

# **STIC Search Report**

## **Biotech-Chem Library**

**STIC Database Tracking Number: 122366**

**TO: Ganapathy Krishnan**  
**Location: REM-5C25/5C18**  
**Art Unit: 1623**  
**Friday, May 21, 2004**  
**Case Serial Number: 10/627920**

**From: Paul Schulwitz**  
**Location: Biotech-Chem Library**  
**REM-1A65**  
**Phone: (571)272-2527**

**paul.schulwitz@uspto.gov**

### **Search Notes**

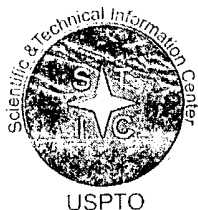
Examiner Krishnan,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Paul Schulwitz  
Technical Information Specialist  
STIC Biotech/Chem Library  
(571)272-2527



# STIC SEARCH RESULTS FEEDBACK FORM

## Biotech-Chem Library

Questions about the scope or the results of the search? Contact *the searcher or contact*:

Mary Hale, Information Branch Supervisor  
571-272-2507 Remsen E01 D86

## Voluntary Results Feedback Form

➤ I am an examiner in Workgroup:  Example: 1610

➤ Relevant prior art **found**, search results used as follows:

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

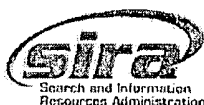
- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature  
(journal articles, conference proceedings, new product announcements etc.)

➤ Relevant prior art **not found**:

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library Remsen Bldg.



Paul

122366

# SEARCH REQUEST FORM

Requestor's Name: Ganapathy Krishnan Serial Number: 101627920  
Date: 5/18/04 Phone: 2-0654 Art Unit: 1623  
Eff: SC25 MR: 5C18

## Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

Search for:

1. Water Soluble Starch that has amylopectin content over 85% by weight and purity, an inflection! Said starch can be as microparticles (cl. 43) and is also a carrier for a protein (cl. 45).
2. ~~Please search cl 47~~  
Please search the process steps of claim 47.

## STAFF USE ONLY

| Date completed: _____        | Search Site         | Vendors            |
|------------------------------|---------------------|--------------------|
| Searcher: _____              | _____ STIC          | _____ IG           |
| Terminal time: _____         | _____ CM-1          | <u>497.75</u> STN  |
| Elapsed time: _____          | _____ Pre-S         | _____ Dialog       |
| CPU time: _____              | Type of Search      | _____ APS          |
| Total time: _____ 20         | _____ N.A. Sequence | _____ Geninfo      |
| Number of Searches: _____ 60 | _____ A.A. Sequence | _____ SDC          |
| Number of Databases: _____   | _____ Structure     | _____ DARC/Questel |
|                              | _____ Bibliographic | _____ Other        |

# Inventor Search

Krishnan 10/627,920

May 21, 2004

L65 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2003:757024 HCAPLUS  
 DOCUMENT NUMBER: 139:265766  
 TITLE: **Starch** microparticles containing a  
 biologically active substance  
 INVENTOR(S): Reslow, Mats; **Jonsson, Monica**; Larsson,  
 Karin; **Laakso, Timo**  
 PATENT ASSIGNEE(S): Swed.  
 SOURCE: U.S. Pat. Appl. Publ., 20 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2003180371 | A1   | 20030925 | US 2002-162674  | 20020606 |
| WO 2003080033 | A1   | 20031002 | WO 2003-SE463   | 20030320 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI,  
 FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,  
 KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,  
 MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,  
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW,  
 AM, AZ, BY, KG  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,  
 NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
 GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: SE 2002-873 A 20020321  
 SE 2002-1599 A 20020530

AB A process for producing microparticles, in which an aqueous solution of  
 purified

**amylopectin-based starch** of reduced mol. weight is prepared,  
 the solution is combined with biol. active substance, an emulsion of  
**starch** droplets is formed in an outer phase of polymer solution, the  
**starch** droplets are made to gel, the gelled **starch**  
 particles are dried, and a release-controlling shell is optionally applied  
 to the particles, wherein at least one buffer substance having the ability  
 of keeping the pH of the produced microparticles above 3 if exposing the  
 microparticles to an aqueous environment is added at any stage during the  
 process. Microparticles which essentially consist of this **starch**  
 , have an amino acid content of less than 50 µg, have no covalent chemical  
 crosslinking and have the activity of keeping the pH above 3 if exposed to  
 a aqueous environment. For example, **starch** microparticles were  
 prepared from highly branched **starch** with average mol. weight of 530 kDa  
 and polyethylene glycol in histidine buffer (pH 6.4).

L65 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2002:391500 HCAPLUS  
 DOCUMENT NUMBER: 136:391006  
 TITLE: Parenterally administrable microparticles containing  
 PEG and **starch**  
 INVENTOR(S): Reslow, Mats; **Joensson, Monica**; **Laakso,**  
**Timo**  
 PATENT ASSIGNEE(S): Bioglan AB, Swed.  
 SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2002039985   | A1   | 20020523 | WO 2001-SE2166  | 20011005 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |      |          |                 |          |
| SE 2000004218   | A    | 20020517 | SE 2000-4218    | 20001116 |
| SE 518008   | C2   | 20020813 |                 |          |
| AU 2001092527   | A5   | 20020527 | AU 2001-92527   | 20011005 |
| US 2002081336   | A1   | 20020627 | US 2001-970649  | 20011005 |
| EP 1333814  | A1   | 20030813 | EP 2001-972893  | 20011005 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                 |          |
| JP 2004513914   | T2   | 20040513 | JP 2002-542360  | 20011005 |
| PRIORITY APPLN. INFO.:<br>SE 2000-4218 A 20001116<br>US 2001-260496P P 20010108<br>WO 2001-SE2166 W 20011005  |      |          |                 |          |
| AB A process for producing microparticles containing biol. active substance, in which process an aqueous solution of the said substance is prepared, this solution is mixed with an aqueous solution of PEG such that the substance is concentrated and/or solidified, the substance is optionally washed, the substance is mixed with an aqueous <b>starch</b> solution, the composition obtained is mixed, after the admixt. of the <b>starch</b> solution, with a polymer solution, thereby forming an emulsion of <b>starch</b> droplets in the polymer solution, the <b>starch</b> droplets are solidified into microparticles, the droplets are solidified into microparticles, the microparticles are dried and a release-controlling shell is optionally applied to these. A procedure for the production of highly concentrated/pptd human growth hormone suitable for immobilization with PEG is given. |      |          |                 |          |
| REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT   |      |          |                 |          |
| L65 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN<br>ACCESSION NUMBER: 2002:276035 HCAPLUS<br>DOCUMENT NUMBER: 136:296466<br>TITLE: Forming purified <b>starch</b> and microparticles with controlled release of a biologically active substance<br>INVENTOR(S): Gustafsson, Nils Ove; Berden, Per; Joensson, Monica; Laakso, Timo; Reslow, Mats<br>PATENT ASSIGNEE(S): Bioglan AB, Swed.<br>SOURCE: PCT Int. Appl., 42 pp.<br>CODEN: PIXXD2   |      |          |                 |          |

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE        |
|---|------|----------|-----------------|-------------|
| WO 2002028909   | A1   | 20020411 | WO 2001-SE2168  | 20011005    |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG |      |          |                 |             |
| SE 2000003616   | A    | 20020407 | SE 2000-3616    | 20001006    |
| SE 517422   | C2   | 20020604 |                 |             |
| AU 2001094460   | A5   | 20020415 | AU 2001-94460   | 20011005    |
| US 2002045745   | A1   | 20020418 | US 2001-970648  | 20011005    |
| US 6689389  | B2   | 20040210 |                 |             |
| US 2002065411   | A1   | 20020530 | US 2001-970795  | 20011005    |
| US 6616948  | B2   | 20030909 |                 |             |
| EP 1325035  | A1   | 20030709 | EP 2001-975101  | 20011005    |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                 |             |
| JP 2004510846   | T2   | 20040408 | JP 2002-532491  | 20011005    |
| US 2003206961   | A1   | 20031106 | US 2003-461393  | 20030616    |
| US 2004019014   | A1   | 20040129 | US 2003-627920  | 20030728    |
| PRIORITY APPLN. INFO.:  |      |          |                 |             |
|   |      |          | SE 2000-3616    | A 20001006  |
|   |      |          | US 2001-260491P | P 20010108  |
|   |      |          | US 2001-970648  | A3 20011005 |
|   |      |          | US 2001-970795  | A3 20011005 |
|   |      |          | WO 2001-SE2168  | W 20011005  |
| AB Production of purified, parenterally administrable <b>starch</b> by washing <b>starch</b> containing >85% <b>amylopectin</b> to remove surface-localized proteins, lipids and endotoxins, subjecting the <b>starch</b> to a mol. weight reduction by acid hydrolysis, and optionally removing residual water-soluble proteins.   |      |          |                 |             |
| REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT   |      |          |                 |             |

L65 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2002:276034 HCAPLUS  
 DOCUMENT NUMBER: 136:296465  
 TITLE: Pharmaceutically acceptable **starch**  
 INVENTOR(S): Gustavsson, Nils Ove; Berden, Per; Joensson, Monica; Laakso, Timo; Reslow, Mats  
 PATENT ASSIGNEE(S): Bioglan AB, Swed.  
 SOURCE: PCT Int. Appl., 43 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2002028908   | A1   | 20020411 | WO 2001-SE2163  | 20011005 |
| W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
| SE 2000003616   | A    | 20020407 | SE 2000-3616    | 20001006 |
| SE 517422   | C2   | 20020604 |                 |          |
| AU 2001094457   | A5   | 20020415 | AU 2001-94457   | 20011005 |
| US 2002045745   | A1   | 20020418 | US 2001-970648  | 20011005 |
| US 6689389  | B2   | 20040210 |                 |          |
| US 2002065411   | A1   | 20020530 | US 2001-970795  | 20011005 |
| US 6616948  | B2   | 20030909 |                 |          |
| EP 1325034  | A1   | 20030709 | EP 2001-975098  | 20011005 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                 |          |
| JP 2004510845   | T2   | 20040408 | JP 2002-532490  | 20011005 |
| US 2003206961   | A1   | 20031106 | US 2003-461393  | 20030616 |
| US 2004019014   | A1   | 20040129 | US 2003-627920  | 20030728 |

## PRIORITY APPLN. INFO.:

|                 |    |          |
|-----------------|----|----------|
| SE 2000-3616    | A  | 20001006 |
| US 2001-260491P | P  | 20010108 |
| US 2001-970648  | A3 | 20011005 |
| US 2001-970795  | A3 | 20011005 |
| WO 2001-SE2163  | W  | 20011005 |

AB Production of purified, parenterally administrable **starch** is accomplished by washing **starch** containing more than 85% **amylopectin** in order to remove surface-localized proteins, lipids and endotoxins, dissolving the **starch** in aqueous medium, mol. weight reduction by shearing, and optionally removal of residual water-soluble proteins, preferably by anion exchange chromatog.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:275775 HCAPLUS

DOCUMENT NUMBER: 136:284479

TITLE: A controlled-release **starch** microparticle for parenteral administration

INVENTOR(S): Reslow, Mats; Bjoern, Soeren; Drustrup, Joern; Gustafsson, Nils Ove; Joensson, Monica; Laakso, Timo

PATENT ASSIGNEE(S): Bioglan AB, Swed.

SOURCE: PCT Int. Appl., 69 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

WO 2002028375 A1 20020411 WO 2001-SE2165 20011005  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, VZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
SE 2000003614 A 20020407 SE 2000-3614 20001006  
SE 517610 C2 20020625  
AU 2001094459 A5 20020415 AU 2001-94459 20011005  
EP 1328258 A1 20030723 EP 2001-975100 20011005  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
JP 2004510730 T2 20040408 JP 2002-532200 20011005  
US 2002102311 A1 20020801 US 2002-970792 20020110  
PRIORITY APPLN. INFO.: SE 2000-3614 A 20001006  
US 2001-260495P P 20010108  
WO 2001-SE2165 W 20011005  
AB A parenterally administrable, biodegradable microparticle preparation, preferably composed of **amylopectin**-containing **starch** is described. The preparation contains a biol. active substance which, during the first 24 h after injection, exhibits a release of the active substance that is less than 25% of the total release, determined from a concentration-time curve in the form of the ratio between the area under the curve during the said first 24 h and the total area under the curve in question. For example, bovine serum albumin (BSA) was immobilized with high loading in **starch** microspheres produced from highly branched, sheared **starch**. A **starch** solution (40%) of sheared, highly branched **starch** with an average mol. weight of 1600 kDa, a solution of PEG 20,000 Da (38%) and a solution of BSA (14%) were prepared in 50 mM sodium phosphate, pH 8.3 and spray dried. The protein yield was 94%, the **starch** yield 89%, and the loading obtained was 10%. The mean particle size was 98  $\mu$ m and with less than 10% of the distribution below 35  $\mu$ m. By incubation with  $\alpha$ -amylase or  $\alpha$ -amylase and amyloglucosidase the microspheres were fully dissolved within 48 h.  
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2002:275771 HCAPLUS  
DOCUMENT NUMBER: 136:299676  
TITLE: Vaccine composition comprising an immunologically active substance embedded in microparticles consisting of **starch** with reduced molecular weight  
INVENTOR(S): Joensson, Monica; Larsson, Karin; Gustafsson, Nils Ove; Laakso, Timo; Reslow, Mats  
PATENT ASSIGNEE(S): Bioglan AB, Swed.  
SOURCE: PCT Int. Appl., 61 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE        |
|---|------|----------|-----------------|-------------|
| WO 2002028371   | A1   | 20020411 | WO 2001-SE2169  | 20011005    |
| W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,<br>CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES,<br>FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,<br>KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,<br>MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL,<br>TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,<br>KG, KZ, MD, RU<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,<br>DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,<br>BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG |      |          |                 |             |
| SE 2000003615   | A    | 20020407 | SE 2000-3615    | 20001006    |
| SE 517421   | C2   | 20020604 |                 |             |
| AU 2001092529   | A5   | 20020415 | AU 2001-92529   | 20011005    |
| US 2002044976   | A1   | 20020418 | US 2001-970793  | 20011005    |
| US 6706288  | B2   | 20040316 |                 |             |
| EP 1322290  | A1   | 20030702 | EP 2001-972895  | 20011005    |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,<br>IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  |      |          |                 |             |
| JP 2004510724   | T2   | 20040408 | JP 2002-531997  | 20011005    |
| US 2002098203   | A1   | 20020725 | US 2002-970794  | 20020110    |
| US 2003211167   | A1   | 20031113 | US 2003-461445  | 20030616    |
| US 6692770  | B2   | 20040217 |                 |             |
| PRIORITY APPLN. INFO.:  |      |          |                 |             |
|   |      |          | SE 2000-3615    | A 20001006  |
|   |      |          | US 2001-260455P | P 20010108  |
|   |      |          | US 2001-970793  | A3 20011005 |
|   |      |          | WO 2001-SE2169  | W 20011005  |
| AB A vaccine composition is disclosed which comprises an immunol. active substance<br>embedded in microparticles essentially consisting of <b>starch</b><br>having an <b>amylopectin</b> content exceeding 85 % by weight, of which at<br>least 80 % by weight has an average mol. weight within the range of 10-10,000<br>kDa.<br>A process for preparing such vaccine composition is also disclosed.  |      |          |                 |             |
| REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS<br>RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT  |      |          |                 |             |
| L65 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN  |      |          |                 |             |
| ACCESSION NUMBER: 2002:275770 HCAPLUS   |      |          |                 |             |
| DOCUMENT NUMBER: 136:299729   |      |          |                 |             |
| TITLE: Biodegradable controlled release microparticles<br>containing <b>amylopectin</b> -based <b>starch</b><br>of reduced molecular weight   |      |          |                 |             |
| INVENTOR(S): Joensson, Monica; Gustavsson, Nils<br>Ove; Laakso, Timo; Reslow, Mats  |      |          |                 |             |
| PATENT ASSIGNEE(S): Bioglan AB, Swed.   |      |          |                 |             |
| SOURCE: PCT Int. Appl., 62 pp.<br>CODEN: PIXXD2   |      |          |                 |             |
| DOCUMENT TYPE: Patent   |      |          |                 |             |
| LANGUAGE: English   |      |          |                 |             |
| FAMILY ACC. NUM. COUNT: 2   |      |          |                 |             |
| PATENT INFORMATION:   |      |          |                 |             |

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO 2002028370  | A1   | 20020411 | WO 2001-SE2164  | 20011005 |
| W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, |      |          |                 |          |

CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES,  
FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,  
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL,  
TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,  
KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

SE 2000003615 A 20020407 SE 2000-3615 20001006

SE 517421 C2 20020604

AU 2001094458 A5 20020415 AU 2001-94458 20011005

US 2002044976 A1 20020418 US 2001-970793 20011005

US 6706288 B2 20040316

EP 1322291 A1 20030702 EP 2001-975099 20011005

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004510723 T2 20040408 JP 2002-531996 20011005

US 2002098203 A1 20020725 US 2002-970794 20020110

US 2003211167 A1 20031113 US 2003-461445 20030616

US 6692770 B2 20040217

PRIORITY APPLN. INFO.:

SE 2000-3615 A 20001006

US 2001-260455P P 20010108

US 2001-970793 A3 20011005

WO 2001-SE2164 W 20011005

AB A process for producing parenterally administrable microparticles, in which an at least 20% by weight aqueous solution of purified **amylopectin**-based **starch** of reduced mol. weight is prepared, the solution is combined with a biol. active substance, an emulsion of **starch** droplets is formed in an outer phase of polymer solution, the **starch** droplets are made to gel, and the gelled **starch** particles are dried. A release-controlling shell is optionally also applied to the particles. Microparticles which essentially consist of the **starch**, have an amino acid content of <50 µg and have no covalent chemical crosslinking. Thus, **starch** microspheres containing BSA were produced from highly branched **starch** with average mol. weight of 1930 kDA. The **starch** solution was mixed with PEG and the mixture was administered s.c. and i.m. to rats. The microspheres were biodegraded rapidly within 1 wk, and the tissue is rapidly normalized.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:372239 HCAPLUS

DOCUMENT NUMBER: 126:347307

TITLE: Sustained-release microparticles containing polymers

INVENTOR(S): Gustafsson, Nils-Ove; Laakso, Timo  
; Fyhr, Peter; Joensson, Monica

PATENT ASSIGNEE(S): Biogram Ab, Swed.; Gustafsson, Nils-Ove; Laakso, Timo;  
Fyhr, Peter; Joensson, Monica

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

WO 9714408 A1 19970424 WO 1996-SE1091 19960903  
W: AL, AM, AT, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ,  
DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP, KE,  
KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,  
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, TJ, TM, TR, TT,  
UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,  
IE, IT, LU, MC, NL, PT  
SE 9503672 A 19970420 SE 1995-3672 19951019  
SE 505146 C2 19970630  
AU 9673478 A1 19970507 AU 1996-73478 19960903  
AU 699080 B2 19981119  
EP 869774 A1 19981014 EP 1996-935641 19960903  
EP 869774 B1 20021204  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI  
JP 2000501380 T2 20000208 JP 1997-515728 19960903  
IL 124052 A1 20001121 IL 1996-124052 19960903  
EP 1142569 A2 20011010 EP 2001-117830 19960903  
EP 1142569 A3 20030521  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI  
AT 228826 E 20021215 AT 1996-935641 19960903  
PT 869774 T 20030430 PT 1996-935641 19960903  
ES 2125209 T3 20030701 ES 1996-935641 19960903  
CZ 293059 B6 20040114 CZ 1998-1173 19960903  
NO 9801558 A 19980406 NO 1998-1558 19980406  
US 6120787 A 20000919 US 1998-51709 19980417  
HK 1011182 A1 20030606 HK 1998-112027 19981116  
PRIORITY APPLN. INFO.: SE 1995-3672 A 19951019  
EP 1996-935641 A3 19960903  
WO 1996-SE1091 W 19960903  
AB Parenterally administrable sustained-release microparticles, are prepared from core particles in an organic solvent-free aqueous medium and an entrapped drug. The core particles are dried and coated with a release-controlling polymer by an air suspension technique so as to create a shell on the core particles without any detrimental exposure of the active substance to an organic solvent. Thus, a coating solution was prepared from Resomer RG756 200, triacetin 10, and acetone 3123 g. **Starch** microparticles (500 g) containing 3.5% BSA were coated with the above solution

L65 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1989:101642 HCAPLUS

DOCUMENT NUMBER: 110:101642

TITLE: Biodegradable microspheres. XII: Properties of the crosslinking chains in polyacryl **starch** microparticles

AUTHOR(S): Stjaernkvist, Peter; Laakso, Timo; Sjoeholm, Ingvar

CORPORATE SOURCE: Dep. Drugs, Natl. Board of Health Welfare, Uppsala, S-751 25, Swed.

SOURCE: Journal of Pharmaceutical Sciences (1989), 78(1), 52-6  
CODEN: JPMSAE; ISSN: 0022-3549

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Polyacryl **starch** microparticles are under current investigation for use as lysosomotropic drug carriers. Some in vivo and in vitro properties of the crosslinking polymer chains in these particles are described. A radioactive label was introduced into the microparticle crosslinks by copolymn. of [14C]acrylamide. It was shown by gel permeation chromatog. that the amount of tetramethylethylenediamine (TEMED)

used in the microparticle polymerization affected the mol. weight composition of the hydrocarbon chains. Increasing the TEMED concentration resulted in a higher proportion of shorter polymeric chains. After i.v. administration to mice, the microparticles were taken up mainly by the liver. Although presumably nonmetabolizable, a slow elimination (terminal half-life of 4-5 mo) of the hydrocarbon chains from the liver was observed. After exocytosis from the Kupffer cells or after their turnover, dissolved material is taken up by liver parenchymal cells and excreted into the bile.

L65 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1988:210046 HCAPLUS

DOCUMENT NUMBER: 108:210046

TITLE: Biodegradable microspheres. X: Some properties of polyacryl **starch** microparticles prepared from acrylic acid-esterified **starch**

AUTHOR(S): Laakso, Timo; Sjöholm, Ingvar

CORPORATE SOURCE: Div. Pharm., Natl. Board of Health and Welfare, Uppsala, S-751 25, Swed.

SOURCE: Journal of Pharmaceutical Sciences (1987), 76(12), 935-9

CODEN: JPMSAE; ISSN: 0022-3549

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Acrylic acid-esterified **starch** was produced by reacting **starch** with acrylic acid chloride. This reaction was rapid and easy to control. Introduction of acrylic groups into **starch** reduced the enzymic degradability of **starch** (e.g., with 12 acrylic groups/100 glucose residues, .apprx.75% of the degradation products eluted before glucose on gel filtration). The degradability could be increased to a large extent by preincubation at pH 5.5 in vitro (e.g., after 16 wk, the corresponding figure was .apprx.15%). The acrylic acid-esterified **starch** was used to prepare polyacryl **starch** microparticles. These were rapidly eliminated from the circulation after i.v. injection in mice, mainly by uptake in the liver. The elimination of the microparticles from the liver, monitored with [<sup>14</sup>C] **starch**, displayed a half-life of .apprx.3.5-4.5 mo. After 5 and 6 mo, .apprx.30% of the initial radioactivity remained in the liver. This is equivalent to the amount anticipated from the enzymic degradation of the monomer

(acrylic acid-esterified **starch**) in vitro and the innate nondegradability of the <sup>14</sup>C-marker. These results, taken together, indicate that the ester bond between **starch** and the hydrocarbon chain in polyacryl **starch** microparticles is hydrolyzed at lysosomal pH.

L65 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1988:137771 HCAPLUS

DOCUMENT NUMBER: 108:137771

TITLE: Biodegradable microspheres. VII: Alterations in mouse liver morphology after intravenous administration of polyacryl **starch** microparticles with different biodegradability

AUTHOR(S): Laakso, Timo; Edman, Peter; Brunk, Ulf

CORPORATE SOURCE: Dep. Pharm. Biochem., Univ. Uppsala, Uppsala, Swed.

SOURCE: Journal of Pharmaceutical Sciences (1988), 77(2), 138-44

CODEN: JPMSAE; ISSN: 0022-3549

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The possible adverse effects, reflected as morphol. alterations, of i.v. administration of polyacryl **starch** microparticles (as drug carriers) were studied in mice. The spleen, lungs, and kidneys displayed a normal morphol. after microparticle administration, while dose-dependent reversible alterations of the liver morphol. were observed. The alterations initially consisted of vacuolization of the hepatocytes along the sinusoids, followed by unicellular hepatocyte necrosis and formation of granulomas. Later, an increased number of mitotic cells reflected tissue generation and, after two weeks, the tissue morphol. was essentially normalized, with the exception of an increased number of binucleated hepatocytes. After repeated administration of the particles in low doses, the same types of alterations were observed but the kinetics of tissue repair was slower. Possible mechanisms inducing these alterations are discussed and comparisons are made with the effects of synthetic polyacrylamide microparticles.

L65 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1988:43953 HCAPLUS

DOCUMENT NUMBER: 108:43953

TITLE: Biodegradable microspheres. VIII. Killing of Leishmania donovani in cultured macrophages by microparticle-bound primaquine

AUTHOR(S): Stjaernkvist, Peter; Artursson, Per; Brunmark, Anders; Laakso, Timo; Sjoeholm, Ingvar

CORPORATE SOURCE: Dep. Drugs, Natl. Board Health Welfare, Uppsala, S-751 25, Swed.

SOURCE: International Journal of Pharmaceutics (1987), 40(3), 215-22

CODEN: IJPHDE; ISSN: 0378-5173

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Primaquine (PQ) covalently bound to polyacryl **starch** microparticles kills L. donovani in cultured mouse peritoneal macrophages. The drug was derivatized with a tetrapeptide spacer and the derivative (Ala-Leu-Ala-Leu-PQ) coupled to the microparticles. This drug-carrier complex did not kill free promastigotes in suspension, but was effective against amastigotes in cultured mouse peritoneal macrophages. Lysosomal processing of the drug-carrier complex is necessary to liberate the pharmacol. active drug. The possible role of reactive oxygen intermediates for the antileishmaniasis effect was discussed.

L65 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1987:642532 HCAPLUS

DOCUMENT NUMBER: 107:242532

TITLE: Biodegradable microspheres. Part IX. Polyacryl **starch** microparticles as a delivery system for the antileishmanial drug, sodium stibogluconate

AUTHOR(S): Baillie, A. J.; Coombs, G. H.; Dolan, T. F.; Hunter, C. A.; Laakso, T.; Sjoeholm, I.; Stjaernkvist, P.

CORPORATE SOURCE: Dep. Pharm., Univ. Strathclyde, Glasgow, G1 1XW, UK

SOURCE: Journal of Pharmacy and Pharmacology (1987), 39(10), 832-5

CODEN: JPPMAB; ISSN: 0022-3573

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Liver parasite burdens of Leishmania donovani in the mouse were determined after treatment with i.v. administration of Na stibogluconate in the free

or carrier form. The carrier form, in which the drug was covalently bound to polyacryl **starch** microparticles, was up to 100-fold more effective than the free form in this murine model of visceral leishmaniasis. Empty microparticles had no effect on liver parasite burdens and the enhanced in-vivo antileishmanial activity of the carrier form of the drug was apparently due to passive drug delivery to the infected liver.

L65 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1987:428308 HCAPLUS

DOCUMENT NUMBER: 107:28308

TITLE: Cellular distribution in rat liver of intravenously administered polyacryl **starch** and chondroitin sulfate microparticles

AUTHOR(S): Laakso, Timo; Smedsrod, Baard

CORPORATE SOURCE: Dep. Drugs, Natl. Board Health Welfare, Uppsala, Swed.

SOURCE: International Journal of Pharmaceutics (1987), 36(2-3), 253-62

CODEN: IJPHDE; ISSN: 0378-5173

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The interaction of polyacryl **starch** and chondroitin sulfate (CS) microparticles with rat liver cells was studied in vivo and in cell cultures. Kupffer cells (KC) in culture avidly engulfed both **starch** and CS particles. Cultured liver endothelial cells (LEC) bound CS, and to a lesser degree **starch** particles. Parenchymal cells (PC) in culture did not bind any of the particles. I.v. injection of either type of particles labeled with fluorescein isothiocyanate, and subsequent isolation of the liver cells showed uptake only in KC. After i.v. administration of <sup>14</sup>C-labeled particles, radioactivity was accumulated mainly in KC. Thus, polysaccharide microparticles in the micron range may be suitable for targeting drugs to KC.

L65 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1987:412756 HCAPLUS

DOCUMENT NUMBER: 107:12756

TITLE: Biodegradable microspheres. VI: Lysosomal release of covalently bound antiparasitic drugs from **starch** microparticles

AUTHOR(S): Laakso, Timo; Stjaernkvist, Peter; Sjoeholm, Ingvar

CORPORATE SOURCE: Dep. Drugs, Natl. Board Health and Welfare, Uppsala, S-751 25, Swed.

SOURCE: Journal of Pharmaceutical Sciences (1987), 76(2), 134-40

CODEN: JPMSAE; ISSN: 0022-3549

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The possibilities of using polyacryl **starch** microparticles as a carrier for low mol. weight drugs were investigated. Two drugs containing primary amino groups, primaquine and trimethoprim, were covalently coupled to the **starch** microparticles via tri-, tetra-, and pentapeptide spacer arms. The drug-particle complexes were prepared by coupling different drug-peptide derivs. to the particles after activation of the **starch** with carbonyldiimidazole. The activation process with subsequent removal of activated groups did not change the degradability of the **starch** microparticles. The resulting drug-carrier complexes were stable in serum, while free drugs were released in a lysosome fraction. Thus, the microparticle-peptide-drug conjugates fulfill the

basic requirements for a drug carrier used to target drugs to the lysosomes (e.g., for the treatment of lysosomal parasitic diseases).

L65 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1987:90045 HCAPLUS

DOCUMENT NUMBER: 106:90045

TITLE: Biodegradable microspheres. IV: Factors affecting the distribution and degradation of polyacryl starch microparticles

AUTHOR(S): Laakso, Timo; Artursson, Per; Sjoeholm, Ingvar

CORPORATE SOURCE: Div. Pharm., Natl. Board Health Welfare, Uppsala, S-751 25, Swed.

SOURCE: Journal of Pharmaceutical Sciences (1986), 75(10), 962-7

CODEN: JPMSAE; ISSN: 0022-3549

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Distribution and elimination of polyacryl starch microparticles (as lysosomotropic drug carriers) after i.v. administration in mice were studied. The half-life of the particles in the circulation is short (<5 min) and they are efficiently taken up by the reticuloendothelial (RES) system, mainly in the liver (50-90%). The stability of the particles, as studied both in vitro (with serum and lysosome prepsns.) and in vivo (via the elimination from the liver), depends on two factors, the amount of initiator of the polymerization process [(N,N,N',N'-tetramethylethylenediamine) (TEMED)] [110-18-9] and the degree of derivatization of the starch. TEMED, used for the polymerization of the acryl groups forming the hydrocarbon chains, detrs. the number and the length of the crosslinks between the starch mols. Large amts. of TEMED induce the formation of particles with many and short crosslinks, which are easily degraded and dissolved in serum and more rapidly eliminated from the liver. The stability in serum can be improved by coadministration of soluble starch [9005-25-8]. Prolonged treatment of the starch with acrylic acid glycidyl ester leads to a high degree of derivatization and, consequently, to less degradable particles remaining in the lysosomes of the RES. The extent of biodegrdn. of the polyacryl starch particles could be anticipated from in vitro degradation of the monomers (acryloylated starch) with amyloglucosidase [9032-08-0].

L65 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1985:84348 HCAPLUS

DOCUMENT NUMBER: 102:84348

TITLE: Characterization of polyacryl starch microparticles as carriers for proteins and drugs

AUTHOR(S): Artursson, Per; Edman, Peter; Laakso, Timo; Sjoeholm, Ingvar

CORPORATE SOURCE: Dep. Drugs, Natl. Board Health Welfare, Uppsala, S-751 25, Swed.

SOURCE: Journal of Pharmaceutical Sciences (1984), 73(11), 1507-13

CODEN: JPMSAE; ISSN: 0022-3549

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Biodegradable microparticles of crosslinked hydroxyethyl starch [9005-27-0] or maltodextrin [9050-36-6] were designed as carriers of proteins and low mol. weight drugs in vivo. The synthesis of acryloyloxyhydroxypropyl derivs. of the polysaccharides and their polymerization

to microparticles are described. The polysaccharides were immobilized in the microparticles in high yields, i.e., up to 40% of the dry weight consisted of the immobilized protein. The optimal conditions of immobilization were investigated by varying the concentration of polysaccharides,

the concentration of acryloyl groups, and the amount of addnl. crosslinking agent.

Exclusion of the crosslinking agent gave maximal immobilization of the macromols. Enzyme kinetics, release profiles, surface localization, and heat stability of the immobilized macromols. are also presented. Microparticles based on **starch** with small amts. of acryloyl groups were completely degraded after incubation with amyloglucosidase. The degradation of microparticles in serum and in the target organelle, the lysosome, was investigated in vitro. The polyacrylic **starch** microspheres (mean diameter, 0.5  $\mu$ m) constitute an attractive alternative to other drug and enzyme carriers.

L65 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1983:595307 HCAPLUS  
DOCUMENT NUMBER: 99:195307  
TITLE: Determination of the degree of derivatization of acryloylated polysaccharides by Fourier transform proton NMR spectroscopy  
AUTHOR(S): Lepistoe, Matti; Artursson, Per; Edman, Peter; **Laakso, Timo**; Sjoeholm, Ingvar  
CORPORATE SOURCE: Div. Pharm., Natl. Board Health Welfare, Uppsala, S-751 25, Swed.  
SOURCE: Analytical Biochemistry (1983), 133(1), 132-5  
CODEN: ANBCA2; ISSN: 0003-2697  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Dextran, glycogen, hydroxyethyl **starch**, and maltodextrin were derivatized with acrylic acid glycidyl ester at alkaline pH. The degree of derivatization was determined by water-elimination Fourier transform NMR and compared with a bromination method. The signals from the anomeric protons of the glucose residues were used as an internal standard and the degree of derivatization was obtained from the relation between the integrated signals from the acrylic and anomeric protons. The NMR technique is more precise and convenient for the determination of acryloyl groups than the bromination method.

L65 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1964:472177 HCAPLUS  
DOCUMENT NUMBER: 61:72177  
ORIGINAL REFERENCE NO.: 61:12564d-e  
TITLE: The fight against potato scurf (*Streptomyces scabies*) through disinfection of the soil with PCNB  
AUTHOR(S): **Gustafsson, Nils**  
CORPORATE SOURCE: Inst. Vaestforskn., Nyaeshamm, Swed.  
SOURCE: Kgl. Skogs-Lantbruksakad. Tidskr. (1962), 101, 301-16  
From: CZ 1964(15), Abstr. No. 1978.  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable

AB Through broad-scattering, harrowing-in or furrow-scattering, PCNB in quantities of 30, 60, and 120 kg./ha. is applied for pretreatment of the soil of potato fields. The protective action of PCNB against potato scurf rises with the dosage. Localization of PCNB in the furrows of the field does not improve the protective action. Minor decreases in yield are attributable to delayed plant development caused by PCNB, as well as

occasional reduction in the contents of **starch** and dry substance. Larger PCNB doses may cause a decline of the boiling quality and affect the taste of potatoes and cause an inclination to discolor. It is recommended, therefore, to restrict application to 50-80 kg/. ha.

L65 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1957:43929 HCAPLUS

DOCUMENT NUMBER: 51:43929

ORIGINAL REFERENCE NO.: 51:8220a-c

TITLE: The influence of potato virus X on yield, tuber size, and chemical composition of the tubers

AUTHOR(S): Emilsson, Borge; Gustafsson, Nils

CORPORATE SOURCE: Inst. Plant Research Cold Storage, Nynashamn, Swed.

SOURCE: Acta. Agr. Scand. (1956), 6, 369-82

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB Potato varieties Bintje, grown in the south and middle of the country, and Eigenheimer, grown in the north, were infected with either a very mild, Xm, or a medium severe, Xy, strain of virus X. The yields were compared with controls at a very early and normal harvest time. In Bintje Xy decreased the yield by 16.8% and Xm by 20.1, and in the Eigenheimer Xy decreased it by 13.9. The immature harvest showed less effect on yield, indicating the differences caused by infection develop mainly during the final stages of growth. In Bintje Xm caused less severe leaf symptoms than Xy but decreased the yield more. Environmental conditions influenced the virus effect. Both strains of X-infection reduced the average tuber size in both varieties and caused a slight reduction in the content of dry matter and **starch** while increasing the N content of the tubers.

L65 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1953:58108 HCAPLUS

DOCUMENT NUMBER: 47:58108

ORIGINAL REFERENCE NO.: 47:9832f-i

TITLE: Photographic polymeric pyrazolone couplers

INVENTOR(S): Allen, Charles F. H.; Laakso, Thomas T. M.

PATENT ASSIGNEE(S): Eastman Kodak Co.

DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|------|
| US 2646421 |      | 19530721 | US              |      |

US 2646421 19530721 US

AB The preparation of polymeric pyrazolone color-forming couplers are described. Thus, to prepare the K salt of p-(3-methyl-5-oxo-1-pyrazolinyl)styrene-maleic acid copolymer (I), 50 parts of p-aminostyrene-maleic acid copolymer (cf. C.A. 36, 4043.4) were dissolved in 500 parts of 50% AcOH containing 38 parts of concentrated HCl. The mixture was cooled to 0° and aqueous

NaNO<sub>2</sub> (20%) was slowly added until a slight excess was present (test with **starch**-iodide paper). The diazonium solution was slowly added to a cold, well-stirred solution of 85 parts SnCl<sub>2</sub> in 500 parts of 50% AcOH

containing

75 parts of concentrated HCl. The hydrazino derivative, while still in the reaction

mass, was mixed with excess NaOAc to combine with residual mineral acid.

To the mixture 26 parts Et acetoacetate (II) was added and the mixture was heated overnight with stirring. The mass was precipitated by pouring into 3

vols. of acetone, the precipitate was washed twice with 1 volume portions of acetone, then H<sub>2</sub>O. After dissolving in dilute K<sub>2</sub>CO<sub>3</sub> and filtering through felt, the solution contained 4% of I by weight. I combines with 2-amino-5-diethylaminotoluene-HCl in the presence of an oxidizing agent to give an intense magenta color. Instead of II there may be used Et ethoxyiminopropionate, Et benzoylacetate, Et oxalacetate, Et anisoylacetate, and Et ethoxyiminopropionate followed by BzCl.

L65 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1950:53755 HCAPLUS

DOCUMENT NUMBER: 44:53755

ORIGINAL REFERENCE NO.: 44:10235i,10236a-c

TITLE: Control of late blight of potatoes. V. Experiments with haulm-killing chemicals in 1949

AUTHOR(S): Emilsson, Borje; Gustafsson, Nils

CORPORATE SOURCE: Inst. Vaxtforskning Kyllagring, Nynashamn, Swed.

SOURCE: Kgl. Lantbruksakad. Tid. (1949), 89, 130-152

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C.A. 43, 9336f. Haulm killing by chemicals decreased the total yield of potatoes but increased the number of marketable size. Most satisfactory results were obtained when the haulms were already somewhat matured. Resistance of the potato skin to injury increased proportionately to the length of time the potatoes were left in the ground after spraying. Haulm killing increased the resistance of the skin to mech. damage and decreased water loss from potatoes during storage. Haulm killing was advantageous economically in the varieties Bintje, Early Puritan, President, and Up to Date but resulted in a loss with Arran Consul. Up to Date showed the greatest advantage. Dry matter and **starch** content were higher in all varieties when the haulms were killed 8 days before harvest than when they were killed 16, 24, or 32 days before. H<sub>2</sub>SO<sub>4</sub> (10% by volume) killed haulms more rapidly and incompletely than did EWOS 936. Other materials tested were B&TS, a dinitrophenol preparation, which gave results similar to those with EWOS 936, Stirpan, which contained dinitro-o-cresol, Santobrite, which contained Na pentachlorophenol. All of the compds. are effective enough to give practical control. Compds. which kill leaves and stalks effectively also decreased the amount of blight.

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FILE COVERS 1907 - 21 May 2004 VOL 140 ISS 22  
FILE LAST UPDATED: 20 May 2004 (20040520/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que 132

|     |        |                          |        |                                      |
|-----|--------|--------------------------|--------|--------------------------------------|
| L7  | 204    | SEA FILE=REGISTRY ABB=ON | PLU=ON | AMYLOPECTIN?/CN                      |
| L9  | 1      | SEA FILE=REGISTRY ABB=ON | PLU=ON | STARCH/CN                            |
| L23 | 1066   | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | (L7 OR L9) (L) PHARMAC?              |
| L24 | 38     | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | L23 AND ?AMYLOPECTIN?                |
| L26 | 699597 | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | INJECT? OR ?PARENTERAL? OR INTRAVEN? |
| L27 | 3      | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | L24 AND L26                          |
| L29 | 92     | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | ?AMYLOPECTIN? AND L26                |
| L30 | 18     | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | L29 AND PHARMAC?                     |
| L32 | 18     | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | L30 OR L27                           |

=> d que 137

|     |     |                          |        |  |
|-----|-----|--------------------------|--------|--|
| L7  | 204 | SEA FILE=REGISTRY ABB=ON | PLU=ON | AMYLOPECTIN?/CN  |
| L9  | 1   | SEA FILE=REGISTRY ABB=ON | PLU=ON | STARCH/CN  |
| L36 | 13  | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | (L7 OR L9) (S) CARRIER(S) (PROTEI N OR AMINO ACID OR PEPTID? OR POLYPEPT?) |
| L37 | 1   | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | L36 AND (MICROPART? OR MICRO? (2A) PARTICL?)                               |

=> d que 149

|     |        |                          |        |   |
|-----|--------|--------------------------|--------|---|
| L9  | 1      | SEA FILE=REGISTRY ABB=ON | PLU=ON | STARCH/CN   |
| L26 | 699597 | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | INJECT? OR ?PARENTERAL? OR INTRAVEN?  |
| L46 | 1      | SEA FILE=REGISTRY ABB=ON | PLU=ON | AMYLOPECTIN/CN  |
| L47 | 216    | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | (L9 OR L46) (L) PUR/RL  |
| L48 | 17     | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | L47 AND (ION? OR ANION? OR CATION?) (2A) ?EXCHANG?                                |
| L49 | 3      | SEA FILE=HCAPLUS ABB=ON  | PLU=ON | L48 AND (L26 OR PHARMAC? OR VACCIN? OR IMMUN? OR (MICRO? AND ?PARTICL?) OR DRUG?) |

=> s 132 or 137 or 149

L50 20 L32 OR L37 OR L49

=&gt; d 150 ibib ab hitind 1-20

L50 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:252369 HCAPLUS

DOCUMENT NUMBER: 140:269531

TITLE: Autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss in human and animal

INVENTOR(S): Boving, Tine Elisabeth Gottschalk; Klysner, Steen

PATENT ASSIGNEE(S): Pharmexa A/s, Den.

SOURCE: PCT Int. Appl., 83 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO 2004024183  | A1   | 20040325 | WO 2003-DK592   | 20030912 |
| <p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM</p> <p>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG</p> |      |          |                 |          |

PRIORITY APPLN. INFO.: DK 2002-1345 A 20020912  
US 2002-410164P P 20020912

AB Disclosed are novel methods that generally rely on immunization against autologous ghrelin. Immunization is preferably effected by administration of analogs of autologous ghrelin, said analogs being capable of inducing antibody production against the autologous ghrelin polypeptides. Especially preferred as an immunogen is autologous ghrelin, which has been modified by introduction of one single or a few foreign, immunodominant and promiscuous T-cell epitopes. Also disclosed are nucleic acid vaccination against ghrelin and vaccination using live vaccines as well as methods and means useful for the vaccination. Such methods and means include methods for the preparation of analogs and **pharmaceutical** formulations, as well as nucleic acid fragments, vectors, transformed cells, polypeptides and **pharmaceutical** formulations.

ICM A61K039-39

ICS A61K039-385; A61K039-00; C07K014-435; A61P003-04

CC 15-2 (Immunochemistry)

Section cross-reference(s): 3, 63

IT Drug delivery systems

(injections, i.m.; autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT Drug delivery systems

(injections, i.p.; autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against

obesity and excess body fat increase or loss)

IT Drug delivery systems  
(**injections**, s.c.; autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT Drug delivery systems  
(**parenterals**; autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

IT 541-59-3, Maleimide 1398-61-4, Chitin 7693-46-1, p-Nitrophenyl chloroformate 8063-16-9, Psyllium 9000-01-5, Gum arabic 9000-07-1, Carrageenan 9000-21-9, Furcellaran 9000-28-6, Gum ghatti 9000-30-0, Guar 9000-40-2, Locust bean gum 9000-65-1, Tragacanth 9000-69-5, Pectin 9002-84-0, Polytetrafluoroethylene 9002-89-5, Poly(vinyl alcohol) 9002-98-6, PEI 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-39-8, Poly(vinyl pyrrolidone) 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 9005-25-8, Starch, biological studies 9005-32-7D, Alginic acid, derivs. 9005-79-2, Glycogen, biological studies 9011-14-7, Poly(methyl methacrylate) 9012-36-6, Agarose 9012-72-0, Glucan 9012-76-4, Chitosan 9014-63-5, Xylan 9036-88-8, Mannan 9037-22-3, **Amylopectin** 9057-02-7, Pullulan 11078-30-1, Galactomannan 11138-66-2, Xanthan 12619-70-4D, Cyclodextrin, derivs. 24937-78-8, Poly(ethylene-co-vinyl acetate) 25087-26-7, Polymethacrylic acid 25249-16-5, Poly(2-hydroxyethyl methacrylate) 25322-68-3D, Polyethylene glycol, derivs. 26780-50-7D, Poly(lactide-co-glycolide), derivs. 37294-28-3, Xyloglucan 51751-43-0D, vinylene derivs. 54991-89-8, Tamarine 83869-56-1, GM-CSF 110865-71-9, Acetan

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(autologous ghrelin and encoding nucleic acid and foreign T cell epitope conjugates for vaccination against obesity and excess body fat increase or loss)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:892567 HCAPLUS

DOCUMENT NUMBER: 139:386334

TITLE: Production of monomeric calicheamicin derivative cytotoxic drug/carrier conjugates

INVENTOR(S): Kunz, Arthur; Moran, Justin Keith; Rubino, Joseph Thomas; Jain, Neera; Vidunas, Eugene Joseph; Simpson, John McLean; Robbins, Paul David; Merchant, Nishith; Dijoseph, John Francis; Ruppen, Mark Edward; Damle, Nitin Krishnaji; Popplewell, Andrew George; et al.

PATENT ASSIGNEE(S): Wyeth Holdings Corporation, USA

SOURCE: PCT Int. Appl., 186 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2003092623 | A2   | 20031113 | WO 2003-US13910 | 20030502 |
| WO 2003092623 | A3   | 20040318 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,  
 PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,  
 TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,  
 MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,  
 NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,  
 GW, ML, MR, NE, SN, TD, TG

US 2004082764 A1 20040429 US 2003-428894 20030502

PRIORITY APPLN. INFO.: US 2002-377440P P 20020502

AB The present invention relates to methods for. the production of monomeric cytotoxic drug/carrier conjugates (the "conjugates") with higher drug loading and substantially reduced low conjugate fraction (LCF). Cytotoxic drug derivative/antibody conjugates, compns. comprising the conjugates and uses of the conjugates are also described. Particularly, the invention relates to anti-CD22 antibody-monomeric calicheamicin conjugates. The invention also relates to the conjugates of the invention, to methods of purification of the conjugates, to **pharmaceutical** compns. comprising the conjugates, and to uses of the conjugates.

IC ICM A61K

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 15

IT Drug delivery systems

(**injections**, i.p.; production of monomeric calicheamicin derivative cytotoxic drug/carrier conjugates)

IT Drug delivery systems

(**injections**, i.v.; production of monomeric calicheamicin derivative cytotoxic drug/carrier conjugates)

IT Drug delivery systems

(**injections**, intraarterial; production of monomeric calicheamicin derivative cytotoxic drug/carrier conjugates)

IT Drug delivery systems

(**injections**, intramedullar; production of monomeric calicheamicin derivative cytotoxic drug/carrier conjugates)

IT Drug delivery systems

(**injections**, intrathecal; production of monomeric calicheamicin derivative cytotoxic drug/carrier conjugates)

IT Drug delivery systems

(**injections**, s.c.; production of monomeric calicheamicin derivative cytotoxic drug/carrier conjugates)

IT Drug delivery systems

(**injections**, transcutaneous; production of monomeric calicheamicin derivative cytotoxic drug/carrier conjugates)

IT Drug delivery systems

(**injections**, transdermal; production of monomeric calicheamicin derivative cytotoxic drug/carrier conjugates)

IT 50-69-1, Ribose 50-70-4, Sorbitol, uses 50-81-7, Ascorbic acid, uses 50-99-7, Glucose, uses 56-81-5, Glycerol, uses 56-82-6, Glyceraldehyde 57-48-7, Fructose, uses 57-50-1, Sucrose, uses 58-86-6, Xylose, uses 59-05-2, Methotrexate 59-23-4, Galactose, uses 63-42-3, Lactose 65-42-9, Lyxose 69-65-8, Mannitol 69-79-4, Maltose 77-86-1, Tromethamine 87-79-6, Sorbose 87-89-8, Inositol 89-65-6, Isoascorbic acid 99-20-7, Trehalose 107-21-1, Ethylene glycol, uses 114-04-5, Neuraminic acid 115-77-5, Pentaerythritol, uses 147-81-9, Arabinose 526-95-4, Gluconic acid 551-84-8, Xylulose 685-73-4, Galacturonic acid 1398-61-4, Chitin 1758-51-6, Erythrose 2152-76-3, Idose 3416-24-8, Glucosamine 3458-28-4, Mannose 5556-48-9, Ribulose 5987-68-8,

Altrose 6038-51-3, Allose 6556-12-3, Glucuronic acid 6814-36-4, Mannuronic acid 7535-00-4, Galactosamine 7647-14-5, Sodium chloride, uses 9000-07-1, Carrageenan 9000-69-5, Pectins 9004-34-6, Cellulose, uses 9004-54-0, Dextran 40,, uses 9004-61-9, Hyaluronic acid 9005-25-8, Starch, uses 9005-32-7, Alginic acid 9005-65-6, Polysorbate 80, 9005-79-2, Glycogen, uses 9005-82-7, Amylose 9007-27-6, Chondroitin 9012-36-6, Agarose 9012-72-0, Glucan 9013-95-0, Levan 9014-63-5, Xylans 9036-88-8, Mannan 9037-22-3, **Amylopectin** 9037-55-2, Galactan 9037-90-5, Fructan 9046-38-2, Galacturonan 9046-40-6, Pectic acid 9057-02-7, Pullulan 9060-75-7, Arabinan 9072-19-9, Fucoidan 11138-66-2, Xanthan gum 17598-81-1, Tagatose 19163-87-2, Gulose 23140-52-5, Psicose 25322-68-3, Polyethylene glycol 25322-69-4, Polypropylene glycol 25525-21-7, Glucaric acid 29884-64-8, Threose 30077-17-9, Talose 37331-28-5, Pustulan 40031-31-0, Erythrulose 53106-52-8, Pentose 60495-58-1, Galactocarolose 64612-25-5, Fucan 71927-65-6, Heptose 75634-40-1, Dermatan 93780-23-5, Hexose 169799-44-4, Keratin 199297-32-0, Pentose

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)  
(production of monomeric calicheamicin derivative cytotoxic drug/carrier conjugates)

L50 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:242150 HCAPLUS

DOCUMENT NUMBER: 138:276257

TITLE: Controlled release compositions containing opioids and polymers

INVENTOR(S): Fischer, Gina; Bar-Shalom, Daniel; Slot, Lillian; Jensen, Christine

PATENT ASSIGNEE(S): Egalet A/S, Den.

SOURCE: PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND   | DATE     | APPLICATION NO. | DATE     |
|---------------|--|----------|-----------------|----------|
| WO 2003024430 | A1   | 20030327 | WO 2002-DK619   | 20020923 |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |

PRIORITY APPLN. INFO.: DK 2001-1376 A 20010921

AB A **pharmaceutical** composition for controlled release of an active substance. The active substance is released into an aqueous medium by erosion of at least one surface of the composition. The composition comprises a matrix containing polymer or a mixture of polymers, an active substance and, optionally, 1 or more excipients, and a coating. A zero order drug release is desirable. The matrix typically comprises PEG and the active substance is typically an opioid such as morphine or a glucuronide. The coating comprises a first cellulose derivative which is substantially insol.

in the aqueous medium and at least 1 of a second cellulose derivative which is soluble or dispersible in water, a plasticizer, and, a filler. A composition was

prepared from the following ingredients: PEG-200,000 83.5, and morphine sulfate 16.5% by weight. The coating and the matrix were prepared as described above. The composition was 9 mm long and had elliptic formed surfaces. Morphine sulfate (96.65%) was released in 8 h.

IC ICM A61K009-28

ICS A61K047-00; A61K009-22; A61K031-485

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

IT Molding of plastics and rubbers

(**injection**; controlled release compns. containing opioids and polymers)

IT Natural products, **pharmaceutical**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(opium; controlled release compns. containing opioids and polymers)

IT 50-21-5, Lactic acid, biological studies 50-69-1, Ribose 50-70-4, Sorbitol, biological studies 50-81-7, Vitamin C, biological studies 50-99-7, Glucose, biological studies 56-84-8, Aspartic acid, biological studies 56-86-0, Glutamic acid, biological studies 57-03-4, Glycerophosphoric acid 57-11-4, Stearic acid, biological studies 57-42-1, Meperidine 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 58-86-6, Xylose, biological studies 62-53-3, Aniline, biological studies 62-54-4, Calcium acetate 62-67-9, Nalorphine 63-42-3, Lactose 64-18-6, Formic acid, biological studies 64-19-7, Acetic acid, biological studies 64-39-1, Promedol 65-42-9, Lyxose 65-85-0, Benzoic acid, biological studies 69-65-8, Mannitol 75-15-0, Carbon disulfide, biological studies 76-41-5, Oxymorphone 76-42-6, Oxycodone 76-57-3, Codeine 76-58-4, Ethylmorphine 76-99-3, Methadone 77-07-6, Levorphanol 77-14-5, Proheptazine 77-15-6, Ethoheptazine 77-20-3, Alphaprodine 77-86-1, Tris(hydroxymethyl)aminomethane 77-92-9, Citric acid, biological studies 79-10-7, Acrylic acid, biological studies 79-14-1, Glycolic acid, biological studies 87-69-4, Tartaric acid, biological studies 87-89-8, Inositol 87-99-0, Xylitol 88-99-3D, Phthalic acid, esters 90-64-2, Mandelic acid 98-10-2, Benzenesulfonamide 98-95-3, Nitrobenzene, biological studies 100-02-7, p-Nitrophenol, biological studies 109-97-7, Pyrrole 110-15-6, Succinic acid, biological studies 110-16-7, Maleic acid, biological studies 110-17-8, Fumaric acid, biological studies 110-44-1, Sorbic acid 110-94-1, Glutaric acid 111-16-0, Pimelic acid 111-42-2, Diethanolamine, biological studies 112-72-1, Myristyl alcohol 112-92-5, Stearyl alcohol 117-81-7, Dioctyl Phthalate 123-56-8, Succinimide 123-76-2, Levulinic acid 124-04-9, Adipic acid, biological studies 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 127-08-2, Potassium acetate 127-09-3, Sodium acetate 127-17-3, Pyruvic acid, biological studies 127-35-5, Phenazocine 140-99-8, Calcium succinate 141-82-2, Malonic acid, biological studies 143-28-2, Oleyl alcohol 143-52-2, Metopon 144-14-9, Anileridine 144-55-8, Sodium hydrogen carbonate, biological studies 144-62-7, Oxalic acid, biological studies 147-81-9, Arabinose 149-91-7, Gallic acid, biological studies 152-02-3, Levallorphan 288-32-4, Imidazole, biological studies 298-12-4, Glyoxylic acid 298-14-6 302-01-2, Hydrazine, biological studies 302-41-0, Piritramide 357-56-2, Dextromoramide 359-83-1, Pentazocine 427-00-9, Desomorphine 437-38-7, Fentanyl 441-61-2, Ethylmethylthiambutene 463-77-4, Carbamic acid, biological studies 466-40-0, Isomethadone 466-97-7, Normorphine 466-99-9, Hydromorphone 467-18-5, Myrophine 467-83-4, Dipipanone 467-84-5, Phenadoxone 467-85-6, Normethadone 467-86-7, Dioxaphetyl

butyrate 468-07-5, Phenomorphan 468-56-4, Hydroxypethidine 469-62-5,  
 Dextropropoxyphene 469-79-4, Ketobemidone 471-34-1, Calcium carbonate,  
 biological studies 471-47-6, Oxamic acid 473-81-4, Glyceric acid  
 490-79-9, Gentisic acid 497-19-8, Sodium carbonate, biological studies  
 506-87-6, Ammonium carbonate 509-60-4, Dihydromorphine 509-78-4,  
 Dimenoxadol 524-84-5, Dimethylthiambutene 526-94-3, MonoSodium  
 tartrate 545-90-4, Dimepheptanol 546-93-0, Magnesium carbonate  
 557-04-0 561-27-3, Heroin 561-48-8, Norpipanone 561-76-2,  
 Properidine 562-26-5, Phenoperidine 565-63-9, Angelic acid 584-08-7,  
 Potassium carbonate 593-67-9, Ethenamine 597-44-4, Citramalic acid  
 613-78-5,  $\beta$ -Naphthyl salicylate 621-82-9, Cinnamic acid, biological  
 studies 639-48-5, Nicomorphine 868-14-4, MonoPotassium tartrate  
 911-65-9, Etonitazene 994-36-5, Sodium citrate 1310-58-3, Potassium  
 hydroxide (K(OH)), biological studies 1310-73-2, Sodium hydroxide,  
 biological studies 1333-84-2, Aluminum oxide hydrate 1336-21-6,  
 Ammonium hydroxide 1344-28-1, Aluminum oxide, biological studies  
 1531-12-0, Norlevorphanol 1592-23-0, Calcium stearate 1724-02-3,  
 Glutaconic acid 2466-09-3, Pyrophosphoric acid 3164-34-9, Calcium  
 tartrate 3458-28-4, Mannose 3572-80-3, Cyclazocine 3688-85-5,  
 Diapamide 3734-52-9, Metazocine 3861-76-5, Clonitazene 4468-02-4,  
 Zinc gluconate 5987-68-8, Altrose 6038-51-3, Allose 6915-15-7, Malic  
 acid 7429-90-5D, Aluminum, compds. 7447-40-7, Potassium chloride  
 (KCl), biological studies 7558-79-4, DiSodium hydrogen phosphate  
 7558-80-7, Sodium dihydrogen phosphate 7601-54-9, TriSodium phosphate  
 7631-86-9, Silica, biological studies 7632-05-5, Sodium phosphate  
 7647-01-0, Hydrochloric acid, biological studies 7647-14-5, Sodium  
 chloride, biological studies 7664-38-2, Orthophosphoric acid, biological  
 studies 7664-38-2D, Phosphoric acid, esters 7664-93-9, Sulfuric acid,  
 biological studies 7693-13-2, Calcium citrate 7733-02-0, Zinc sulfate  
 7757-82-6, Sodium sulfate, biological studies 7757-93-9, DiCalcium  
 phosphate 7758-11-4, Potassium monohydrogen phosphate 7778-18-9,  
 Calcium sulfate 7778-49-6, Potassium citrate 7778-77-0, Potassium  
 dihydrogen phosphate 7778-80-5, Potassium sulfate, biological studies  
 7786-30-3, Magnesium chloride (MgCl<sub>2</sub>), biological studies 7803-49-8,  
 Hydroxylamine, biological studies 9000-28-6, Ghatti gum 9000-69-5,  
 Pectin 9002-18-0, Agar 9003-11-6 9004-32-4, Carboxymethyl cellulose  
 9004-34-6, Cellulose, biological studies 9004-34-6D, Cellulose, derivs.  
 9004-35-7, Cellulose acetate 9004-38-0, Cellulose acetate phthalate  
 9004-48-2, Cellulose propionate 9004-53-9, Dextrin 9004-54-0, Dextran,  
 biological studies 9004-57-3, Ethyl Cellulose 9004-58-4, Ethyl  
 hydroxyethyl Cellulose 9004-59-5, Ethyl methyl Cellulose 9004-62-0,  
 Hydroxyethyl Cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3,  
 HPMC 9004-67-5, Methyl Cellulose 9004-70-0, Cellulose nitrate  
 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid  
 9005-35-0, Calcium Alginate 9005-38-3, Sodium Alginate 9005-82-7,  
 Amylose 9014-63-5, Xylan 9032-42-2, Hydroxyethyl methyl Cellulose  
 9037-22-3, **Amylopectin** 10043-35-3, Boric acid, biological  
 studies 10043-52-4, Calcium chloride, biological studies 10061-32-2,  
 Levophenacylmorphan 10103-46-5, Calcium phosphate 10316-66-2,  
 2-Hydroxy-2-cyclohexenone 10343-62-1, Metaphosphoric acid 13463-67-7,  
 Titanium oxide, biological studies 13495-09-5, Piminodine 14047-56-4  
 14297-87-1, Benzylmorphine 14807-96-6, Talc, biological studies  
 15301-48-1, Bezitramide 15686-91-6, Propiram 16068-46-5, Potassium  
 phosphate 20290-09-9, Morphine 3-glucuronide 20290-10-2, Morphine  
 6-glucuronide 20594-83-6, Nalbuphine 22445-04-1 25322-68-3,  
 Polyethylene glycol 25322-68-3D, Polyethylene glycol, esters or ethers  
 25384-17-2, Allylprodine 27203-92-5, Tramadol 30435-30-4 36653-82-4,  
 Cetyl alcohol 37353-59-6, HydroxyMethyl Cellulose 42408-82-2,  
 Butorphanol 51931-66-9, Tilidine 52485-79-7, Buprenorphine

53648-55-8, Dezocine 54340-58-8, Meptazinol 56030-54-7, Sufentanil  
 61380-40-3, Lofentanil 62212-91-3, Sodium Starch 69670-80-0,  
 Hydroxymethyl propyl cellulose 71195-58-9, Alfentanil 72522-13-5,  
 Eptazocine 74811-65-7, Croscarmellose sodium 106392-12-5, Polyethylene  
 glycol-polypropylene glycol block copolymer 154326-36-0, Glycolic  
 acid-lactic acid-polyethylene glycol block copolymer 443360-37-0  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(controlled release comps. containing opioids and polymers)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:242149 HCAPLUS

DOCUMENT NUMBER: 138:276256

TITLE: Controlled release **pharmaceutical**  
 compositions containing polymers

INVENTOR(S): Fischer, Gina; Bar-Shalom, Daniel; Slot, Lillian;  
 Lademann, Anne-Marie; Jensen, Christine

PATENT ASSIGNEE(S): Egalet A/S, Den.

SOURCE: PCT Int. Appl., 105 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2003024429 | A1   | 20030327 | WO 2002-DK620   | 20020923 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,  
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,  
 KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,  
 MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,  
 SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,  
 ZW, AM, AZ, BY

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
 NE, SN, TD, TG

PRIORITY APPLN. INFO.: DK 2001-1377 A 20010921  
 DK 2002-1044 A 20020703

AB A method for controlling the release of at least one therapeutically,  
 prophylactically and/or diagnostically active substance into an aqueous medium  
 by erosion of at least one surface of a **pharmaceutical** composition  
 The method comprises adjusting the concentration and/or the nature of the  
 ingredients making up the matrix composition in such a manner so as to obtain  
 an approx. zero-order release of the drug from the **pharmaceutical**  
 composition when subject to an in vitro dissoln. test as described herein. The  
 composition comprises a matrix composition containing a polymer or a mixture  
 of polymers

that may be substantially water soluble and/or crystalline, an active substance  
 and, optionally, one or more **pharmaceutically** acceptable  
 excipients, and a coating. Typical polymers are PEG. The coating  
 comprises a first cellulose derivative which is substantially insol. in the  
 aqueous medium, and at least one of a second cellulose derivative which is  
 soluble or

dispersible in water, a plasticizer, and a filler. The active ingredient  
 may be carvedilol. Stable solid dispersions of active substances having

low water solubility are also disclosed. Thus, a composition contained PEG 64.6,

- carvedilol 30, and citric acid 5.4% by weight
- IC ICM A61K009-22
- ICS A61K009-28; A61K047-00; A61K031-403
- CC 63-6 (Pharmaceuticals)
- Section cross-reference(s): 1, 62
- IT Alcohols, biological studies
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (C16-18; controlled release **pharmaceutical** compns. containing polymers)
- IT Viscosity
- (adjusting agents; controlled release **pharmaceutical** compns. containing polymers)
- IT Heart, disease
- (angina pectoris; controlled release **pharmaceutical** compns. containing polymers)
- IT Molding of plastics and rubbers
- (blow; controlled release **pharmaceutical** compns. containing polymers)
- IT Molding of plastics and rubbers
- (compression; controlled release **pharmaceutical** compns. containing polymers)
- IT Antihypertensives
- Antioxidants
- Binders
- Buffers
- Cardiovascular agents
- Coating materials
- Deodorants (personal)
- Diffusion
- Disinfectants
- Dissolution
- Dissolution rate
- Fillers
- Gums and Mucilages
- Human
- Hypertension
- Lubricants
- Molasses
- Molecular weight distribution
- Particle size distribution
- Plasticizers
- Polymorphism (crystal)
- Solubility
- Solubilizers
- Solvents
- Stability
- Stabilizing agents
- (controlled release **pharmaceutical** compns. containing polymers)
- IT Acids, biological studies
- Alkali metal salts
- Alkaline earth salts
- Amides, biological studies
- Amines, biological studies
- Amino acids, biological studies
- Bentonite, biological studies
- Carbohydrates, biological studies
- Carboxylic acids, biological studies

Clays, biological studies  
Disaccharides  
Ethers, biological studies  
Fatty acids, biological studies  
Glycerides, biological studies  
Kaolin, biological studies  
Monosaccharides  
Oligosaccharides, biological studies  
Paraffin oils  
Polymers, biological studies  
Polyoxyalkylenes, biological studies  
Polyoxyalkylenes, biological studies  
Polysaccharides, biological studies  
Salts, biological studies  
Smectite-group minerals  
Vitamins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(controlled release **pharmaceutical** compns. containing polymers)

IT Drug delivery systems  
(controlled-release; controlled release **pharmaceutical**  
compns. containing polymers)

IT Carboxylic acids, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(dicarboxylic; controlled release **pharmaceutical** compns.  
containing polymers)

IT Polyoxyalkylenes, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(esters or ethers; controlled release **pharmaceutical** compns.  
containing polymers)

IT Fatty acids, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(esters; controlled release **pharmaceutical** compns. containing  
polymers)

IT Carrageen (*Chondrus crispus*)  
(exts.; controlled release **pharmaceutical** compns. containing  
polymers)

IT Heart, disease  
(failure; controlled release **pharmaceutical** compns. containing  
polymers)

IT Alcohols, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(fatty; controlled release **pharmaceutical** compns. containing  
polymers)

IT Plantago psyllium  
(husk exts. (Isagbol); controlled release **pharmaceutical**  
compns. containing polymers)

IT Molding of plastics and rubbers  
(**injection**; controlled release **pharmaceutical**  
compns. containing polymers)

IT Bases, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(inorg.; controlled release **pharmaceutical** compns. containing  
polymers)

IT Surfactants  
(nonionic; controlled release **pharmaceutical** compns. containing  
polymers)

IT Carboxylic acids, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(oligo-; controlled release **pharmaceutical** compns. containing

- polymers)
- IT Acids, biological studies  
Bases, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(organic; controlled release **pharmaceutical** compns. containing polymers)
- IT Gums and Mucilages  
(panwar; controlled release **pharmaceutical** compns. containing polymers)
- IT Carboxylic acids, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polycarboxylic; controlled release **pharmaceutical** compns. containing polymers)
- IT Polyoxyalkylenes, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polyester-, block; controlled release **pharmaceutical** compns. containing polymers)
- IT Polyoxyalkylenes, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polyester-, graft; controlled release **pharmaceutical** compns. containing polymers)
- IT Polyesters, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polyoxyalkylene-, block; controlled release **pharmaceutical** compns. containing polymers)
- IT Polyesters, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polyoxyalkylene-, graft; controlled release **pharmaceutical** compns. containing polymers)
- IT Humidity  
(relative; controlled release **pharmaceutical** compns. containing polymers)
- IT Drug delivery systems  
(solid dispersions; controlled release **pharmaceutical** compns. containing polymers)
- IT Carbohydrates, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(sugar esters; controlled release **pharmaceutical** compns. containing polymers)
- IT Diet  
(supplements; controlled release **pharmaceutical** compns. containing polymers)
- IT Drug delivery systems  
(tablets, controlled-release; controlled release **pharmaceutical** compns. containing polymers)
- IT Fats and Glyceridic oils, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(vegetable, hydrogenated; controlled release **pharmaceutical** compns. containing polymers)
- IT Fats and Glyceridic oils, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(vegetable; controlled release **pharmaceutical** compns. containing polymers)
- IT 72956-09-3, Carvedilol  
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(controlled release **pharmaceutical** compns. containing polymers)
- IT 50-21-5, Lactic acid, biological studies 50-69-1, Ribose 50-70-4, Sorbitol, biological studies 50-81-7, Vitamin C, biological studies

50-99-7, Glucose, biological studies 56-84-8, Aspartic acid, biological studies 56-86-0, Glutamic acid, biological studies 57-03-4, Glycerophosphoric acid 57-11-4, Stearic acid, biological studies 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 58-86-6, Xylose, biological studies 59-23-4, Galactose, biological studies 62-53-3, Aniline, biological studies 62-54-4, Calcium acetate 63-42-3, Lactose 64-18-6, Formic acid, biological studies 64-19-7, Acetic acid, biological studies 64-31-3, Morphine sulfate 65-42-9, Lyxose 65-85-0, Benzoic acid, biological studies 69-65-8, Mannitol 75-15-0, Carbon disulfide, biological studies 77-86-1, Tris(hydroxymethyl)aminomethane 77-92-9, Citric acid, biological studies 79-10-7, Acrylic acid, biological studies 79-14-1, Glycolic acid, biological studies 87-69-4, Tartaric acid, biological studies 87-89-8, Inositol 88-99-3D, Phthalic acid, esters 90-64-2, Mandelic acid 98-10-2, Benzenesulfonamide 98-95-3, Nitrobenzene, biological studies 100-02-7, p-Nitrophenol, biological studies 109-97-7, Pyrrole 110-15-6, Succinic acid, biological studies 110-16-7, Maleic acid, biological studies 110-17-8, Fumaric acid, biological studies 110-94-1, Glutaric acid 111-16-0, Pimelic acid 111-42-2, Diethanolamine, biological studies 112-72-1, Myristyl alcohol 112-92-5, Stearyl alcohol 117-81-7, Dioctyl phthalate 123-56-8, Succinimide 123-76-2, Levulinic acid 124-04-9, Adipic acid, biological studies 127-08-2, Potassium acetate 127-09-3, Sodium acetate 127-17-3, Pyruvic acid, biological studies 140-99-8, Calcium succinate 141-82-2, Malonic acid, biological studies 143-28-2, Oleyl alcohol 144-55-8, Sodium hydrogen carbonate, biological studies 144-62-7, Oxalic acid, biological studies 147-81-9, Arabinose 149-91-7, Gallic acid, biological studies 150-90-3, Sodium succinate 288-32-4, Imidazole, biological studies 298-12-4, Glyoxylic acid 298-14-6 302-01-2, Hydrazine, biological studies 463-77-4, Carbamic acid, biological studies 471-34-1, Calcium carbonate, biological studies 471-47-6, Oxamic acid 473-81-4, Glyceric acid 490-79-9, Gentisic acid 497-19-8, Sodium carbonate, biological studies 506-87-6, Ammonium carbonate 546-93-0, Magnesium carbonate 557-04-0 565-63-9, Angelic acid 584-08-7, Potassium carbonate 593-67-9, Ethylenamine 597-44-4, Citramalic acid 613-78-5,  $\beta$ -Naphthyl salicylate 621-82-9, Cinnamic acid, biological studies 676-47-1 868-18-8, Sodium tartrate 921-53-9, Potassium tartrate 994-36-5, Sodium citrate 1310-58-3, Potassium hydroxide (K(OH)), biological studies 1310-73-2, Sodium hydroxide, biological studies 1336-21-6, Ammonium hydroxide 1344-28-1, Aluminum oxide, biological studies 1724-02-3, Glutaconic acid 2152-76-3, Idose 2466-09-3, Pyrophosphoric acid 3164-34-9, Calcium tartrate 3458-28-4, Mannose 4468-02-4, Zinc gluconate 5987-68-8, Altrose 6038-51-3, Allose 6915-15-7, Malic acid 7429-90-5D, Aluminum, compds. 7447-40-7, Potassium chloride, biological studies 7558-79-4, DiSodium hydrogen phosphate 7558-80-7, Sodium dihydrogen phosphate 7601-54-9, TriSodium phosphate 7631-86-9, Silica, biological studies 7632-05-5, Sodium phosphate 7647-01-0, Hydrochloric acid, biological studies 7647-14-5, Sodium chloride, biological studies 7664-38-2, Orthophosphoric acid, biological studies 7664-38-2D, Phosphoric acid, esters 7664-93-9, Sulfuric acid, biological studies 7693-13-2, Calcium citrate 7733-02-0, Zinc sulfate 7757-82-6, Sodium sulfate, biological studies 7757-93-9, DiCalcium phosphate 7758-11-4 7778-18-9, Calcium sulfate 7778-49-6, Potassium citrate 7778-53-2, TriPotassium phosphate 7778-77-0, Potassium dihydrogen phosphate 7778-80-5, Potassium sulfate, biological studies 7786-30-3, Magnesium chloride, biological studies 7803-49-8, Hydroxylamine, biological studies 9000-01-5, Acacia gum 9000-28-6, Ghatti gum 9000-69-5, Pectin 9004-32-4, Carboxymethyl cellulose 9004-32-4D, Carboxymethyl

cellulose, crosslinked 9004-34-6, Cellulose, biological studies  
 9004-34-6D, Cellulose, derivs. 9004-35-7, Cellulose acetate 9004-38-0,  
 Cellulose acetate phthalate 9004-48-2, Cellulose propionate 9004-53-9,  
 Dextrin 9004-54-0, Dextran, biological studies 9004-57-3, Ethyl  
 cellulose 9004-58-4, Ethyl hydroxyethyl cellulose 9004-59-5, Ethyl  
 methyl cellulose 9004-62-0, Hydroxyethyl cellulose 9004-64-2,  
 Hydroxypropyl cellulose 9004-65-3, HPMC 9004-67-5, Methyl cellulose  
 9004-70-0, Cellulose nitrate 9004-99-3, Polyethylene glycol monostearate  
 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid  
 9005-35-0, Calcium Alginate 9005-38-3, Sodium Alginate 9005-82-7,  
 Amylose 9014-63-5, Xylan 9032-42-2, Hydroxyethyl methyl cellulose  
 9037-22-3, **Amylopectin** 10043-35-3, Boric acid,  
 biological studies 10043-52-4, Calcium chloride, biological studies  
 10103-46-5, Calcium phosphate 10316-66-2, 2-Hydroxy-2-cyclohexenone  
 10343-62-1, Metaphosphoric acid 13463-67-7, Titanium oxide, biological  
 studies 14807-96-6, Talc, biological studies 16068-46-5, Potassium  
 phosphate 18859-54-6 19163-87-2, Gulose 21645-51-2, Aluminum oxide  
 trihydrate, biological studies 25322-68-3, Polyethylene glycol  
 25322-68-3D, Polyethylene glycol, esters or ethers 30077-17-9, Talose  
 30435-30-4 36653-82-4, Cetyl alcohol 37353-59-6, Hydroxymethyl  
 cellulose 62212-91-3, Sodium Starch 69670-80-0, Hydroxymethyl propyl  
 cellulose 74811-65-7, Croscarmellose sodium 106392-12-5, Polyethylene  
 glycol-polypropylene glycol block copolymer 154326-36-0, Glycolic  
 acid-lactic acid-polyethylene glycol block copolymer 443360-37-0  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (controlled release **pharmaceutical** compns. containing polymers)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:242148 HCAPLUS

DOCUMENT NUMBER: 138:276255

TITLE: Controlled release solid dispersions containing  
 carvedilol

INVENTOR(S): Fischer, Gina; Bar-Shalom, Daniel; Slot, Lillian;  
 Lademann, Anne-Marie; Jensen, Christine

PATENT ASSIGNEE(S): Egalet A/S, Den.

SOURCE: PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.    | KIND   | DATE     | APPLICATION NO. | DATE     |
|---------------|--|----------|-----------------|----------|
| WO 2003024426 | A1   | 20030327 | WO 2002-DK621   | 20020923 |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |          |

PRIORITY APPLN. INFO.: DK 2001-1375 A 20010921

DK 2001-1611 A 20011031  
 DK 2002-1044 A 20020703

- AB A controlled release **pharmaceutical** composition for oral use comprises a solid dispersion of at least one therapeutical agent and/or diagnostic substance, which at least partially is in an amorphous form, a polymer that has plasticizing properties, and optionally, a stabilizing agent, the at least one active substance having a limited water solubility, and the composition being designed to release the active substance with a substantially zero order release. The polymer is typically a polyethylene glycol and/or polyethylene oxide having a mol. weight of at least about 20,000 in crystalline and/or amorphous form or a mixture of such polymers, and the active substance is typically carvedilol. The composition may comprise a coated matrix, the coating comprising a first cellulose derivative which is substantially insol. in the aqueous medium, and at least one of a second cellulose derivative which is soluble or dispersible in water, a plasticizer, and
- a filler. Thus, a composition contained PEG 64.6, carvedilol 30, and citric acid 5.4% by weight. The dissoln. profile corresponded to a zero-order release of carvedilol from the composition
- IC ICM A61K009-16  
 ICS A61K009-22; A61K009-28; A61K031-403
- CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1, 62
- IT Molding of plastics and rubbers  
 (injection; controlled release solid dispersions containing carvedilol)
- IT 50-21-5, Lactic acid, biological studies 50-69-1, Ribose 50-70-4, Sorbitol, biological studies 50-81-7, Vitamin C, biological studies 50-99-7, Glucose, biological studies 56-84-8, Aspartic acid, biological studies 56-86-0, Glutamic acid, biological studies 57-03-4, Glycerophosphoric acid 57-11-4, Stearic acid, biological studies 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 58-86-6, Xylose, biological studies 59-23-4, Galactose, biological studies 62-53-3, Aniline, biological studies 62-54-4, Calcium acetate 63-42-3, Lactose 64-18-6, Formic acid, biological studies 64-19-7, Acetic acid, biological studies 65-42-9, Lyxose 65-85-0, Benzoic acid, biological studies 69-65-8, Mannitol 75-15-0, Carbon disulfide, biological studies 77-86-1, Tris(hydroxymethyl)aminomethane 77-92-9, Citric acid, biological studies 79-10-7, Acrylic acid, biological studies 79-14-1, Glycolic acid, biological studies 87-69-4, Tartaric acid, biological studies 87-89-8, Inositol 88-99-3D, Phthalic acid, esters 90-64-2, Mandelic acid 98-10-2, Benzenesulfonamide 98-95-3, Nitrobenzene, biological studies 100-02-7, p-Nitrophenol, biological studies 109-97-7, Pyrrole 110-15-6, Succinic acid, biological studies 110-16-7, Maleic acid, biological studies 110-17-8, Fumaric acid, biological studies 110-94-1, Glutaric acid 111-16-0, Pimelic acid 111-42-2, Diethanolamine, biological studies 112-72-1, Myristyl alcohol 112-92-5, Stearyl alcohol 117-81-7, Dioctyl phthalate 123-56-8, Succinimide 123-76-2, Levulinic acid 124-04-9, Adipic acid, biological studies 127-08-2, Potassium acetate 127-09-3, Sodium acetate 127-17-3, Pyruvic acid, biological studies 140-99-8, Calcium succinate 141-82-2, Malonic acid, biological studies 143-28-2, Oleyl alcohol 144-55-8, Sodium hydrogen carbonate, biological studies 144-62-7, Oxalic acid, biological studies 147-81-9, Arabinose 149-91-7, Gallic acid, biological studies 150-90-3, Sodium succinate 288-32-4, Imidazole, biological studies 298-12-4, Glyoxylic acid 298-14-6 302-01-2, Hydrazine, biological studies 463-77-4, Carbamic acid, biological studies 471-34-1, Calcium carbonate, biological studies 471-47-6,

Oxamic acid 473-81-4, Glyceric acid 490-79-9, Gentisic acid 497-19-8, Sodium carbonate, biological studies 506-87-6, Ammonium carbonate 546-93-0, Magnesium carbonate 557-04-0 565-63-9, Angelic acid 584-08-7, Potassium carbonate 593-67-9, Ethylenamine 597-44-4, Citramalic acid 613-78-5,  $\beta$ -Naphthyl salicylate 621-82-9, Cinnamic acid, biological studies 676-47-1 868-18-8, Sodium tartrate 921-53-9, Potassium tartrate 994-36-5, Sodium citrate 1310-58-3, Potassium hydroxide (KOH), biological studies 1310-73-2, Sodium hydroxide, biological studies 1336-21-6, Ammonium hydroxide 1344-28-1, Aluminum oxide, biological studies 1724-02-3, Glutaconic acid 2152-76-3, Idose 2466-09-3, Pyrophosphoric acid 3164-34-9, Calcium tartrate 3458-28-4, Mannose 4468-02-4, Zinc gluconate 5987-68-8, Altrose 6038-51-3, Allose 6915-15-7, Malic acid 7429-90-5D, Aluminum, compds. 7447-40-7, Potassium chloride (KCl), biological studies 7558-79-4, DiSodium hydrogen phosphate 7558-80-7, Sodium dihydrogen phosphate 7601-54-9, TriSodium phosphate 7631-86-9, Silica, biological studies 7632-05-5, Sodium phosphate 7647-01-0, Hydrochloric acid, biological studies 7647-14-5, Sodium chloride, biological studies 7664-38-2, Orthophosphoric acid, biological studies 7664-38-2D, Phosphoric acid, esters 7664-93-9, Sulfuric acid, biological studies 7693-13-2, Calcium citrate 7733-02-0, Zinc sulfate 7757-82-6, Sodium sulfate, biological studies 7757-93-9, DiCalcium phosphate 7758-11-4 7778-18-9, Calcium sulfate 7778-49-6, Potassium citrate 7778-53-2, TriPotassium phosphate 7778-77-0, Potassium dihydrogen phosphate 7778-80-5, Potassium sulfate, biological studies 7786-30-3, Magnesium chloride, biological studies 7803-49-8, Hydroxylamine, biological studies 9000-01-5, Acacia gum 9000-28-6, Ghatti gum 9000-69-5, Pectin 9003-11-6 9004-32-4, Carboxymethyl cellulose 9004-34-6, Cellulose, biological studies 9004-34-6D, Cellulose, derivs. 9004-35-7, Cellulose acetate 9004-38-0, Cellulose acetate phthalate 9004-48-2, Cellulose propionate 9004-53-9, Dextrin 9004-54-0, Dextran, biological studies 9004-57-3, Ethyl cellulose 9004-58-4, Ethyl hydroxyethyl cellulose 9004-59-5, Ethyl methyl cellulose 9004-62-0, Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, HPMC 9004-67-5, Methyl cellulose 9004-70-0, Cellulose nitrate 9004-99-3, Polyethylene glycol monostearate 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9005-35-0, Calcium Alginate 9005-38-3, Sodium Alginate 9005-82-7, Amylose 9014-63-5, Xylan 9032-42-2, Hydroxyethyl methyl cellulose 9037-22-3, **Amylopectin** 10043-35-3, Boric acid, biological studies 10043-52-4, Calcium chloride, biological studies 10103-46-5, Calcium phosphate 10316-66-2, 2-Hydroxy-2-cyclohexenone 10343-62-1, Metaphosphoric acid 13463-67-7, Titanium oxide, biological studies 14807-96-6, Talc, biological studies 16068-46-5, Potassium phosphate 18859-54-6 19163-87-2, Gulose 21645-51-2, Aluminum oxide trihydrate, biological studies 25322-68-3, Polyethylene glycol 25322-68-3D, Polyethylene glycol, esters or ethers 30077-17-9, Talose 30435-30-4 36653-82-4, Cetyl alcohol 37353-59-6, Hydroxymethyl cellulose 62212-91-3, Sodium Starch 69670-80-0, Hydroxymethyl propyl cellulose 72956-44-6, DesmethylCarvedilol 74811-65-7, Croscarmellose sodium 95093-99-5 95094-00-1 106392-12-5, Polyethylene glycol-polypropylene glycol block copolymer 154326-36-0, Glycolic acid-lactic acid-polyethylene glycol block copolymer 443360-37-0

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(controlled release solid dispersions containing carvedilol)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 2002:675881 HCAPLUS  
 DOCUMENT NUMBER: 137:222038  
 TITLE: Carrier systems comprising vitamin B12-biodegradable  
**microparticulate** conjugates for peroral  
 delivery of drugs, peptides/proteins and vaccines  
 INVENTOR(S): Chalasani, Kishore Babu; Diwan, Prakash Vamanrao;  
 Raghavan, Kondapuram Vijaya; Russell-Jones, Gregory  
 John; Jain, Sanjain Kumar; Rao, Kollipara Kotesawa  
 PATENT ASSIGNEE(S): Council of Scientific and Industrial Research, India  
 SOURCE: PCT Int. Appl., 47 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO 2002067995  | A1   | 20020906 | WO 2001-IN27    | 20010226 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,<br>CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,<br>HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,<br>LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,<br>SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,<br>YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,<br>DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,<br>BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG |      |          |                 |          |
| GB 2374010   | A1   | 20021009 | GB 2002-7457    | 20010226 |
| EP 1363672   | A1   | 20031126 | EP 2001-915652  | 20010226 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,<br>IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                 |          |
| US 6482413   | B1   | 20021119 | US 2001-795979  | 20010301 |
| US 2002192235  | A1   | 20021219 |                 |          |

PRIORITY APPLN. INFO.: WO 2001-IN27 A 20010226  
 AB The invention relates to a novel complex for oral delivery of drugs,  
 therapeutic protein / peptides and vaccines which are loaded in a vitamin  
 B12 (VB12) coupled particulate carrier system with spacers in between, the  
 carrier system with spacers having a formula VB12-R1/R2-N wherein, R1 or  
 R2 is spacer and/or agents for derivatization of VB12 to provide either  
 NH2 or COOH or SH groups, and N is the **micro-** or nano-  
**particle** carriers for the delivery of injectable drugs,  
 therapeutic protein/peptides and vaccines. A number of VB12 derivs. were  
 prepared and conjugated to modified polysaccharide derivs. such as starch,  
 chitosan, dextran, or guar gum.  
 IC ICM A61K047-48  
 ICS A61K009-16; A61K009-51  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 26  
 IT Polymers, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (biodegradable; carrier systems comprising vitamin B12-biodegradable  
**microparticulate** conjugates for peroral delivery of drugs,  
 peptides/proteins and vaccines)  
 IT Drug delivery systems  
 (capsules; carrier systems comprising vitamin B12-biodegradable  
**microparticulate** conjugates for peroral delivery of drugs,  
 peptides/proteins and vaccines)  
 IT Cholera

## Vaccines

(carrier systems comprising vitamin B12-biodegradable **microparticulate** conjugates for peroral delivery of drugs, peptides/proteins and vaccines)

IT Polysaccharides, biological studies

RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(carrier systems comprising vitamin B12-biodegradable **microparticulate** conjugates for peroral delivery of drugs, peptides/proteins and vaccines)

IT Interferons

Intrinsic factors

Peptides, biological studies

Polyanhydrides

Polyesters, biological studies

Proteins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(carrier systems comprising vitamin B12-biodegradable **microparticulate** conjugates for peroral delivery of drugs, peptides/proteins and vaccines)

IT Drug delivery systems

(carriers; carrier systems comprising vitamin B12-biodegradable **microparticulate** conjugates for peroral delivery of drugs, peptides/proteins and vaccines)

IT Drug delivery systems

(controlled-release; carrier systems comprising vitamin B12-biodegradable **microparticulate** conjugates for peroral delivery of drugs, peptides/proteins and vaccines)

IT Drug delivery systems

(gels; carrier systems comprising vitamin B12-biodegradable **microparticulate** conjugates for peroral delivery of drugs, peptides/proteins and vaccines)

IT Antigens

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hepatitis B surface; carrier systems comprising vitamin B12-biodegradable **microparticulate** conjugates for peroral delivery of drugs, peptides/proteins and vaccines)

IT Drug delivery systems

(oral; carrier systems comprising vitamin B12-biodegradable **microparticulate** conjugates for peroral delivery of drugs, peptides/proteins and vaccines)

IT Drug delivery systems

(pastes; carrier systems comprising vitamin B12-biodegradable **microparticulate** conjugates for peroral delivery of drugs, peptides/proteins and vaccines)

IT Drug delivery systems

(tablets; carrier systems comprising vitamin B12-biodegradable **microparticulate** conjugates for peroral delivery of drugs, peptides/proteins and vaccines)

IT Vaccines

(typhoid fever; carrier systems comprising vitamin B12-biodegradable **microparticulate** conjugates for peroral delivery of drugs, peptides/proteins and vaccines)

IT 11096-26-7, EPO

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(EPO; carrier systems comprising vitamin B12-biodegradable **microparticulate** conjugates for peroral delivery of drugs, peptides/proteins and vaccines)

IT 100-20-9, Terephthaloyl chloride 106-89-8, Epichlorohydrin, reactions

111-30-8, Glutaraldehyde 530-62-1, 1,1'-Carbonyldiimidazole 693-13-0,  
 N,N'-Diisopropylcarbodiimide 1303-96-4, Borax 1892-57-5, Edac  
 6066-82-6, N-Hydroxysuccinimide 10025-87-3, Phosphorus oxychloride  
 68181-17-9, Spdp 68528-80-3, Disuccinimidyl suberate 70539-42-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)

(carrier systems comprising vitamin B12-biodegradable  
**microparticulate** conjugates for peroral delivery of drugs,  
 peptides/proteins and vaccines)

IT 68-19-9P, Vitamin B12 9004-54-0DP, Dextran, conjugates with vitamin B12  
 derivs. 9005-25-8DP, Starch, conjugates with vitamin B12 derivs.

26264-28-8P 66786-09-2P 160158-24-7P 160158-25-8P 160158-28-1P  
 160177-87-7P 160927-56-0P 160927-59-3P 160927-60-6P 160935-25-1P  
 164728-08-9P 164728-09-0P 164728-10-3P 164728-11-4P 455255-25-1P  
 455255-26-2P 455255-28-4P 455255-34-2P 455255-36-4P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);  
 USES (Uses)

(carrier systems comprising vitamin B12-biodegradable  
**microparticulate** conjugates for peroral delivery of drugs,  
 peptides/proteins and vaccines)

IT 9000-69-5, Pectin 9005-82-7, Amylose 9007-28-7, Chondroitin sulfate  
 RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT

(Reactant or reagent); USES (Uses)

(carrier systems comprising vitamin B12-biodegradable  
**microparticulate** conjugates for peroral delivery of drugs,  
 peptides/proteins and vaccines)

IT 9000-30-0DP, Guar gum, conjugates with vitamin B12 derivs. 9012-76-4DP,  
 Chitosan, conjugates with vitamin B12 derivs.

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)

(carrier systems comprising vitamin B12-biodegradable  
**microparticulate** conjugates for peroral delivery of drugs,  
 peptides/proteins and vaccines)

IT 1403-66-3, Gentamycin 9001-27-8, Factor VIII 9003-16-1, Poly(fumaric  
 acid) 9004-10-8, Insulin, biological studies 9005-49-6, Heparin,  
 biological studies 9011-14-7, Pmma 9034-40-6D, LHRH, analogs  
 13422-51-0, Hydroxycobalamin 13422-52-1, Aquocobalamin 13422-55-4,  
 Methylcobalamin 13870-90-1, Adenosylcobalamin 26780-50-7,  
 Glycolide-lactide copolymer 37517-28-5, Amikacin 52352-27-9,  
 Poly(hydroxybutyric acid) 83869-56-1, GM-CSF 117381-39-2, Fumaric  
 acid-sebacic acid copolymer 143011-72-7, G-CSF

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(carrier systems comprising vitamin B12-biodegradable  
**microparticulate** conjugates for peroral delivery of drugs,  
 peptides/proteins and vaccines)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:276035 HCAPLUS

DOCUMENT NUMBER: 136:296466

TITLE: Forming purified starch and **microparticles**  
 with controlled release of a biologically active  
 substance

INVENTOR(S): Gustafsson, Nils Ove; Berden, Per; Joensson, Monica;  
 Laakso, Timo; Reslow, Mats

PATENT ASSIGNEE(S): Bioglan AB, Swed.

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

| PATENT NO.  | KIND   | DATE     | APPLICATION NO. | DATE     |
|---|--|----------|-----------------|----------|
| WO 2002028909   | A1   | 20020411 | WO 2001-SE2168  | 20011005 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, VZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG |  |          |                 |          |
| SE 2000003616   | A  | 20020407 | SE 2000-3616    | 20001006 |
| SE 517422   | C2   | 20020604 |                 |          |
| AU 2001094460   | A5   | 20020415 | AU 2001-94460   | 20011005 |
| US 2002045745   | A1   | 20020418 | US 2001-970648  | 20011005 |
| US 6689389  | B2   | 20040210 |                 |          |
| US 2002065411   | A1   | 20020530 | US 2001-970795  | 20011005 |
| US 6616948  | B2   | 20030909 |                 |          |
| EP 1325035  | A1   | 20030709 | EP 2001-975101  | 20011005 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |  |          |                 |          |
| JP 2004510846   | T2   | 20040408 | JP 2002-532491  | 20011005 |
| US 2003206961   | A1   | 20031106 | US 2003-461393  | 20030616 |
| US 2004019014   | A1   | 20040129 | US 2003-627920  | 20030728 |
| PRIORITY APPLN. INFO.:<br>SE 2000-3616 A 20001006<br>US 2001-260491P P 20010108<br>US 2001-970648 A3 20011005<br>US 2001-970795 A3 20011005<br>WO 2001-SE2168 W 20011005  |  |          |                 |          |
| AB  | Production of purified, <b>parenterally</b> administrable starch by washing starch containing >85% <b>amylopectin</b> to remove surface-localized proteins, lipids and endotoxins, subjecting the starch to a mol. weight reduction by acid hydrolysis, and optionally removing residual water-soluble proteins. |          |                 |          |
| IC  | ICM C08B030-12<br>ICS C08B030-20; A61K047-36; A61K009-16; A61K009-50   |          |                 |          |
| CC  | 44-6 (Industrial Carbohydrates)  |          |                 |          |
| ST  | starch purified by acid hydrolysis <b>microparticle</b> controlled release; <b>pharmaceutical</b> pure starch manuf  |          |                 |          |
| IT  | Toxins<br>RL: REM (Removal or disposal); PROC (Process)<br>(endotoxins; purified starch and <b>microparticles</b> with controlled release of a biol. active substance)   |          |                 |          |
| IT  | <b>Anion exchange</b><br>(of starch purified of surface-localized proteins)  |          |                 |          |
| IT  | <b>Microparticles</b><br>(purified starch and <b>microparticles</b> with controlled release of a biol. active substance)   |          |                 |          |
| IT  | Lipids, processes<br>Proteins<br>RL: REM (Removal or disposal); PROC (Process)<br>(purified starch and <b>microparticles</b> with controlled release   |          |                 |          |

of a biol. active substance)  
 IT 9005-25-8P, Starch, preparation  
 RL: PUR (Purification or recovery); PREP (Preparation)  
 (from Cerestar C Gel 06090; purified starch and microparticles  
 with controlled release of a biol. active substance)  
 IT 57-55-6, Propylene glycol, uses 64-17-5, Ethanol, uses 67-63-0,  
 Isopropanol, uses 67-64-1, Acetone, uses 107-21-1, Ethylene glycol,  
 uses 1310-73-2, Sodium hydroxide, uses  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (pharmaceutically acceptable starch protein removal by)  
 REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 2002:276034 HCAPLUS  
 DOCUMENT NUMBER: 136:296465  
 TITLE: Pharmaceutically acceptable starch  
 INVENTOR(S): Gustavsson, Nils Ove; Berden, Per; Joensson, Monica;  
 Laakso, Timo; Reslow, Mats  
 PATENT ASSIGNEE(S): Bioglan AB, Swed.  
 SOURCE: PCT Int. Appl., 43 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

| PATENT NO.             | KIND   | DATE     | APPLICATION NO. | DATE        |
|------------------------|--|----------|-----------------|-------------|
| WO 2002028908          | A1   | 20020411 | WO 2001-SE2163  | 20011005    |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MN, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU |          |                 |             |
| RW:                    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG   |          |                 |             |
| SE 2000003616          | A  | 20020407 | SE 2000-3616    | 20001006    |
| SE 517422              | C2   | 20020604 |                 |             |
| AU 2001094457          | A5   | 20020415 | AU 2001-94457   | 20011005    |
| US 2002045745          | A1   | 20020418 | US 2001-970648  | 20011005    |
| US 6689389             | B2   | 20040210 |                 |             |
| US 2002065411          | A1   | 20020530 | US 2001-970795  | 20011005    |
| US 6616948             | B2   | 20030909 |                 |             |
| EP 1325034             | A1   | 20030709 | EP 2001-975098  | 20011005    |
| R:                     | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |          |                 |             |
| JP 2004510845          | T2   | 20040408 | JP 2002-532490  | 20011005    |
| US 2003206961          | A1   | 20031106 | US 2003-461393  | 20030616    |
| US 2004019014          | A1   | 20040129 | US 2003-627920  | 20030728    |
| PRIORITY APPLN. INFO.: |  |          | SE 2000-3616    | A 20001006  |
|                        |  |          | US 2001-260491P | P 20010108  |
|                        |  |          | US 2001-970648  | A3 20011005 |
|                        |  |          | US 2001-970795  | A3 20011005 |
|                        |  |          | WO 2001-SE2163  | W 20011005  |
| AB                     | Production of purified, parenterally administrable starch is   |          |                 |             |

accomplished by washing starch containing more than 85% **amylopectin** in order to remove surface-localized proteins, lipids and endotoxins, dissolving the starch in aqueous medium, mol. weight reduction by shearing, and optionally removal of residual water-soluble proteins, preferably by **anion exchange** chromatog.

IC ICM C08B030-12  
ICS C08B030-20; A61K047-36; A61K009-16; A61K009-50  
CC 44-6 (Industrial Carbohydrates)  
Section cross-reference(s): 63  
ST **pharmaceutical** pure starch manuf; purifn starch **anion exchange**; endotoxin removal starch; lipid removal starch; protein removal starch  
IT Toxins  
RL: REM (Removal or disposal); PROC (Process)  
(endotoxins; manufacture of **pharmaceutically** acceptable starch)  
IT **Anion exchange**  
**Pharmaceutical** industry  
(manufacture of **pharmaceutically** acceptable starch)  
IT Lipids, processes  
Proteins  
RL: REM (Removal or disposal); PROC (Process)  
(manufacture of **pharmaceutically** acceptable starch)  
IT **9005-25-8P**, Starch, preparation  
RL: **PUR (Purification or recovery)**; PREP (Preparation)  
(Cerestar C\*Gel 06090; manufacture of **pharmaceutically** acceptable starch)  
IT 57-55-6, Propylene glycol, uses 64-17-5, Ethanol, uses 67-63-0, Isopropanol, uses 67-64-1, Acetone, uses 107-21-1, Ethylene glycol, uses 1310-73-2, Sodium hydroxide, uses  
RL: NUU (Other use, unclassified); USES (Uses)  
(manufacture of **pharmaceutically** acceptable starch)  
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2002:275771 HCAPLUS  
DOCUMENT NUMBER: 136:299676  
TITLE: **Vaccine** composition comprising an **immunologically** active substance embedded in **microparticles** consisting of starch with reduced molecular weight  
INVENTOR(S): Joensson, Monica; Larsson, Karin; Gustafsson, Nils Ove; Laakso, Timo; Reslow, Mats  
PATENT ASSIGNEE(S): Bioglan AB, Swed.  
SOURCE: PCT Int. Appl., 61 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO 2002028371  | A1   | 20020411 | WO 2001-SE2169  | 20011005 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, |      |          |                 |          |

TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

SE 2000003615 A 20020407 SE 2000-3615 20001006  
 SE 517421 C2 20020604  
 AU 2001092529 A5 20020415 AU 2001-92529 20011005  
 US 2002044976 A1 20020418 US 2001-970793 20011005  
 US 6706288 B2 20040316  
 EP 1322290 A1 20030702 EP 2001-972895 20011005  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 JP 2004510724 T2 20040408 JP 2002-531997 20011005  
 US 2002098203 A1 20020725 US 2002-970794 20020110  
 US 2003211167 A1 20031113 US 2003-461445 20030616  
 US 6692770 B2 20040217

## PRIORITY APPLN. INFO.:

SE 2000-3615 A 20001006  
 US 2001-260455P P 20010108  
 US 2001-970793 A3 20011005  
 WO 2001-SE2169 W 20011005

- AB A **vaccine** composition is disclosed which comprises an **immunol**  
 . active substance embedded in **microparticles** essentially  
 consisting of starch having an amylopectin content exceeding 85 % by weight,  
 of which at least 80 % by weight has an average mol. weight within the range of  
 10-10,000 kDa. A process for preparing such **vaccine** composition is also  
 disclosed.
- IC ICM A61K009-16  
 ICS A61K009-50
- CC 63-3 (Pharmaceuticals)  
 Section cross-reference(s): 15
- ST **vaccine** antigen embedding **microparticle** starch mol wt
- IT Glutamate receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (NMDA-binding; **vaccines**; **vaccine** composition comprising  
 an **immunol**. active substance embedded in  
**microparticles** consisting of starch with reduced mol. weight)
- IT **Immunostimulants**  
 (adjuvants; **vaccine** composition comprising an **immunol**.  
 active substance embedded in **microparticles** consisting of  
 starch with reduced mol. weight)
- IT Sterilization and Disinfection  
 (autoclaving; **vaccine** composition comprising an **immunol**.  
 active substance embedded in **microparticles** consisting of  
 starch with reduced mol. weight)
- IT Polymers, biological studies  
 RL: PEP (Physical, engineering or chemical process); POF (Polymer in  
 formulation); PYP (Physical process); THU (Therapeutic use); BIOL  
 (Biological study); PROC (Process); USES (Uses)  
 (biodegradable; **vaccine** composition comprising an **immunol**  
 . active substance embedded in **microparticles** consisting of  
 starch with reduced mol. weight)
- IT **Drug** delivery systems  
 (emulsions; **vaccine** composition comprising an **immunol**.  
 active substance embedded in **microparticles** consisting of  
 starch with reduced mol. weight)
- IT Toxins  
 RL: REM (Removal or disposal); PROC (Process)  
 (endotoxins; **vaccine** composition comprising an **immunol**.)

- active substance embedded in **microparticles** consisting of starch with reduced mol. weight)
- IT **Drug delivery systems**  
(**injections**, i.m.; **vaccine** composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)
- IT **Drug delivery systems**  
(**injections**, s.c.; **vaccine** composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)
- IT **Encapsulation**  
(**microencapsulation**; **vaccine** composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)
- IT **Drug delivery systems**  
(**microparticles**; **vaccine** composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)
- IT **Drug delivery systems**  
(**microspheres**; **vaccine** composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)
- IT **Drug delivery systems**  
(oral, controlled-release; **vaccine** composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)
- IT **Drying**  
(spray; **vaccine** composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)
- IT **Antigens**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(tumor-specific antigens, **vaccines**; **vaccine** composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)
- IT **Vaccines**  
(tumor; **vaccine** composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)
- IT **Anion exchange chromatography**  
Drying  
Filtration  
Freeze drying  
Human  
    **Immunization**  
    **Immunostimulants**  
    **Ion exchange chromatography**  
Mammalia  
Mixing  
Molecular weight distribution  
Preparative chromatography  
    **Vaccines**  
Washing  
    (**vaccine** composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)
- IT **Polyoxyalkylenes, biological studies**  
RL: PEP (Physical, engineering or chemical process); POF (Polymer in formulation); PYP (Physical process); THU (Therapeutic use); BIOL

(Biological study); PROC (Process); USES (Uses)  
 (vaccine composition comprising an immunol. active substance embedded in microparticles consisting of starch with reduced mol. weight)

IT Lipids, processes  
 Proteins  
 RL: REM (Removal or disposal); PROC (Process)  
 (vaccine composition comprising an immunol. active substance embedded in microparticles consisting of starch with reduced mol. weight)

IT Alums  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccine composition comprising an immunol. active substance embedded in microparticles consisting of starch with reduced mol. weight)

IT Antigens  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccine composition comprising an immunol. active substance embedded in microparticles consisting of starch with reduced mol. weight)

IT Cytokines  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccine composition comprising an immunol. active substance embedded in microparticles consisting of starch with reduced mol. weight)

IT Lipid A  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccine composition comprising an immunol. active substance embedded in microparticles consisting of starch with reduced mol. weight)

IT Oligonucleotides  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccine composition comprising an immunol. active substance embedded in microparticles consisting of starch with reduced mol. weight)

IT Saponins  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccine composition comprising an immunol. active substance embedded in microparticles consisting of starch with reduced mol. weight)

IT Antitumor agents  
 (vaccines; vaccine composition comprising an immunol. active substance embedded in microparticles consisting of starch with reduced mol. weight)

IT DNA  
 Peptides, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (vaccines; vaccine composition comprising an immunol. active substance embedded in microparticles consisting of starch with reduced mol. weight)

IT 9000-90-2,  $\alpha$ -Amylase 9032-08-0, Amyloglucosidase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (vaccine composition comprising an immunol. active substance embedded in microparticles consisting of starch with reduced mol. weight)

IT 9005-27-0, Hydroxyethyl starch  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (vaccine composition comprising an immunol. active

substance embedded in **microparticles** consisting of starch with reduced mol. weight)

IT 25322-68-3, Polyethylene glycol  
 RL: PEP (Physical, engineering or chemical process); POF (Polymer in formulation); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (vaccine composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)

IT 9005-25-8P, Starch, biological studies 9005-82-7P, Amylose  
 9037-22-3P, Amylopectin  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); PUR (**Purification or recovery**); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
 (vaccine composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)

IT 7429-90-5D, Aluminum, salts  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccine composition comprising an **immunol.** active substance embedded in **microparticles** consisting of starch with reduced mol. weight)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:525955 HCAPLUS

DOCUMENT NUMBER: 135:112008

TITLE: Amphiphilic and ionic polymer matrixes and derivatives

INVENTOR(S): thereof for use in **pharmaceutical** vesicles  
 De Miguel, Ignacio; Imbertie, Laurent; Betbeder, Didier; Lescure, Francois; Kravtsoff, Roger

PATENT ASSIGNEE(S): Biovector Therapeutics SA, Fr.

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2001051090 | A2   | 20010719 | WO 2001-FR64    | 20010110 |
| WO 2001051090 | A3   | 20020228 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

|            |    |          |               |          |
|------------|----|----------|---------------|----------|
| FR 2803526 | A1 | 20010713 | FR 2000-329   | 20000112 |
| FR 2803517 | A1 | 20010713 | FR 2000-15126 | 20001123 |

PRIORITY APPLN. INFO.: FR 2000-329 A 20000112  
 FR 2000-15126 A 20001123

AB The invention relates to a novel type of amphiphilic and ionic polymer

matrixes comprising a macromol. hydrophilic matrix bearing a pos. or neg. ionic charge, whereby a lipidic phase having a sign opposite to that of the matrix is incorporated therein. The invention also refers to a method for the production and use thereof. A suspension of amphiphilic submicron vesicles was prepared containing submicron particles 72, dipalmitoyl phosphatidyl choline 1.33, cetyl tri-Me ammonium bromide 0.53, and halofantrine 2 mg/mL. The % incorporation of halofantrine in the vesicles was 100%.

- IC ICM A61K047-36
- ICS A61K007-00; A61K009-00; A23L001-00; A61P031-10; A61P005-30
- CC 63-6 (Pharmaceuticals)
- Section cross-reference(s): 38
- ST amphiphilic ionic polymer **pharmaceutical** vesicle halofantrine
- IT Cardiolipins
  - Fatty acids, biological studies
  - Lipids, biological studies
  - Oligosaccharides, biological studies
  - Phospholipids, biological studies
  - Polysaccharides, biological studies
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (amphiphilic and ionic polymer matrixes and derivs. thereof for use in **pharmaceutical** vesicles)
- IT Surfactants
  - (anionic; amphiphilic and ionic polymer matrixes and derivs. thereof for use in **pharmaceutical** vesicles)
- IT Surfactants
  - (cationic; amphiphilic and ionic polymer matrixes and derivs. thereof for use in **pharmaceutical** vesicles)
- IT Phosphatidylglycerols
  - Phosphatidylserines
  - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (diacyl derivs.; amphiphilic and ionic polymer matrixes and derivs. thereof for use in **pharmaceutical** vesicles)
- IT Drug delivery systems
  - (films; amphiphilic and ionic polymer matrixes and derivs. thereof for use in **pharmaceutical** vesicles)
- IT Drug delivery systems
  - (inhalants; amphiphilic and ionic polymer matrixes and derivs. thereof for use in **pharmaceutical** vesicles)
- IT Drug delivery systems
  - (liposomes; amphiphilic and ionic polymer matrixes and derivs. thereof for use in **pharmaceutical** vesicles)
- IT Drug delivery systems
  - (nanoparticles; amphiphilic and ionic polymer matrixes and derivs. thereof for use in **pharmaceutical** vesicles)
- IT Surfactants
  - (nonionic; amphiphilic and ionic polymer matrixes and derivs. thereof for use in **pharmaceutical** vesicles)
- IT Drug delivery systems
  - (ophthalmic; amphiphilic and ionic polymer matrixes and derivs. thereof for use in **pharmaceutical** vesicles)
- IT Drug delivery systems
  - (parenterals; amphiphilic and ionic polymer matrixes and derivs. thereof for use in **pharmaceutical** vesicles)
- IT Drug delivery systems
  - (solns.; ophthalmic; amphiphilic and ionic polymer matrixes and derivs. thereof for use in **pharmaceutical** vesicles)
- IT Drug delivery systems
  - (tapes; amphiphilic and ionic polymer matrixes and derivs. thereof for

use in **pharmaceutical** vesicles)

IT Drug delivery systems  
(topical; amphiphilic and ionic polymer matrixes and derivs. thereof  
for use in **pharmaceutical** vesicles)

IT Drug delivery systems  
(vaginal; amphiphilic and ionic polymer matrixes and derivs. thereof  
for use in **pharmaceutical** vesicles)

IT 51-84-3, Choline acetate, biological studies 57-09-0, Cetyltrimethyl  
ammonium bromide 63-89-8, Dipalmitoylphosphatidyl choline 106-89-8,  
biological studies 107-43-7D, betaine, esters 302-79-4, Trans-Retinoic  
acid 541-15-1D, Carnitine, acyl derivs. 979-32-8, Estradiol valerate  
1397-89-3, Amphotericin b **9037-22-3, Amylopectin**  
9050-36-6, Maltodextrin 10025-87-3, Phosphoric trichloride 13895-77-7,  
Glycidyl trimethyl ammonium bromide 14357-21-2, Dioctadecyl dimethyl  
ammonium 59865-13-3, Cyclosporin a 69756-53-2, Halofantrine  
124050-77-7, DOGS 144189-73-1, DOTAP  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(amphiphilic and ionic polymer matrixes and derivs. thereof for use in  
**pharmaceutical** vesicles)

L50 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:389122 HCAPLUS

DOCUMENT NUMBER: 129:45340

TITLE: Method of preparing drug-macromolecular complex  
preparations using coordination bond

INVENTOR(S): Ikada, Yoshito; Tabata, Yasuhiko

PATENT ASSIGNEE(S): Seisan Kaihatsu Kagaku Kenkyusho, Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------|------|----------|-----------------|----------|
| JP 10158195            | A2   | 19980616 | JP 1996-354252  | 19961128 |
| PRIORITY APPLN. INFO.: |      |          | JP 1996-354252  | 19961128 |

AB Drugs having chelating ability are mixed with macromol. substances having  
chelating ability or chelating ligands in the presence of metal ions to  
give the title prepsns. DTPA anhydride-modified pullulan having DTPA  
residues at 0.062  $\mu$ mol/mg was mixed with an aqueous solution containing IFN  
and  
ZnCl<sub>2</sub> to give IFN-pullulan chelate complex, which accumulated in the liver  
of mice.

IC ICM A61K047-30

CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 8, 15

IT Drug delivery systems  
(**injections**; drug-macromol. chelate complexes prepsns. for  
drug targeting)

IT Radiosensitizers, biological  
(**pharmaceutical**; drug-macromol. chelate complexes prepsns. for  
drug targeting)

IT 7440-66-6DP, Zinc, chelates with water-soluble macromols. and drugs,  
biological studies 7440-70-2DP, Calcium, chelates with water-soluble  
macromols. and drugs, biological studies 9001-63-2DP, Lysozyme, chelates  
with water-soluble macromols. 9002-89-5DP, Poly(vinyl alcohol), reaction  
products with DTPA anhydride, chelates with drugs 9037-22-3DP,

**Amylopectin**, reaction products with DTPA anhydride, chelates with drugs 9057-02-7DP, Pullulan, reaction products with DTPA anhydride, chelates with drugs 23911-26-4DP, DTPA anhydride, reaction products with water-soluble macromols., chelates with drugs  
RL: BPR (Biological process); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
(drug-macromol. chelate complexes preps. for drug targeting)

L50 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:463833 HCAPLUS

DOCUMENT NUMBER: 127:126466

TITLE: Tumor accumulation of polymers and microgels with different size after **intravenous injection**

AUTHOR(S): Ikada, Y.; Tabata, Y.; Murakami, Y.

CORPORATE SOURCE: Research Center for Biomedical Engineering, Kyoto University, Kyoto, 606, Japan

SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1997), 24th, 777-778

CODEN: PCRMEY; ISSN: 1022-0178

PUBLISHER: Controlled Release Society, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB When variously-sized polymers were i.v. **injected** to tumor-bearing mice, there existed an optimal range of mol. size for high tumor accumulation of the polymers. This can be explained on the basis of **pharmacokinetic** anal. As the mol. size of polymer increased, their accumulation rate at the tumor tissue decreased, while their AUC value increased.

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 1

IT Drug delivery systems

(**injections**, i.v.; tumor accumulation of polymers and microgels with different size after i.v. **injection**)

IT Microgels

Neoplasm

(tumor accumulation of polymers and microgels with different size after i.v. **injection**)

IT Polymers, biological studies

Polyoxyalkylenes, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(tumor accumulation of polymers and microgels with different size after i.v. **injection**)

IT Biological transport

(uptake; tumor accumulation of polymers and microgels with different size after i.v. **injection**)

IT 9002-89-5, Polyvinyl alcohol 9004-54-0, Dextran, biological studies

9037-22-3, **Amylopectin** 25322-68-3, Peg

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(tumor accumulation of polymers and microgels with different size after i.v. **injection**)

L50 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:97244 HCAPLUS

DOCUMENT NUMBER: 126:105683

TITLE: Preparation of aqueous dispersions of particles of crosslinked water-soluble polymers, the particles obtained, and their **pharmaceutical** use

INVENTOR(S): Vanderhoff, John W.; Lu, Cheng Xun; Lee, Clarence C.; Tsai, Chi-Chun

PATENT ASSIGNEE(S): C.R. Bard, Inc., USA; Lehigh University

SOURCE: PCT Int. Appl., 137 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO.   | DATE     |
|--|------|----------|-------------------|----------|
| WO 9639464   | A1   | 19961212 | WO 1996-US10249   | 19960606 |
| W: JP  |      |          |                   |          |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE |      |          |                   |          |
| EP 830416  | A1   | 19980325 | EP 1996-922457    | 19960606 |
| R: BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE, IE                      |      |          |                   |          |
| JP 11507679  | T2   | 19990706 | JP 1996-502262    | 19960606 |
| PRIORITY APPLN. INFO.:   |      |          | US 1995-466676 A  | 19950606 |
|  |      |          | WO 1996-US10249 W | 19960606 |

AB Crosslinked water-soluble polymer particles are prepared by combining an aqueous

solution of a water-soluble polymer, particularly a polysaccharide, with an oil medium so as to form an emulsion of droplets of the water-soluble polymer, and adding to the emulsion a crosslinking agent so as to form crosslinked water-soluble polymer particles. Their use includes administration by **injection** to a patient in need of treatment an aqueous suspension of the water-soluble polymer particles. Thus, an aqueous solution of Na alginate containing XAMA 7 as crosslinking agent at pH 11 was agitated with toluene in the presence of Span 60 to form a water-in-oil emulsion. When the desired droplet size distribution was obtained, the pH was adjusted to 7-8 with HOAC to initiate crosslinking, producing a dispersion of polymer microspheres with diameter <150 µm.

IC ICM C08J003-26

ICS A61L031-00; A61L027-00

CC 44-5 (Industrial Carbohydrates)

Section cross-reference(s): 63

IT 1398-61-4, Chitin 9000-07-1, Carrageenan 9002-89-5, Poly(vinyl alcohol) 9003-39-8, Poly(N-vinylpyrrolidone) 9004-54-0, Dextran, processes 9004-61-9, Hyaluronic acid 9004-62-0, Hydroxyethyl cellulose 9004-65-3, Methocel K 4M 9004-67-5, Methyl cellulose 9005-25-8, Starch, processes 9005-38-3, Sodium alginate 9005-49-6, Heparin sulfate, processes 9005-79-2, Glycogen, processes 9005-82-7, Amylose 9007-28-7, Chondroitin sulfate 9012-36-6, Agarose 9012-76-4, Chitosan 9037-22-3, **Amylopectin** 11138-66-2, Xanthan 24967-94-0, Dermatan sulfate 54724-00-4, Curdlan 142804-65-7, Gellan 169799-44-4, Keratin sulfate

RL: PEP (Physical, engineering or chemical process); PROC (Process)  
(preparation of aqueous dispersions of particles of crosslinked

water-soluble  
polymers)

L50 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1993:415338 HCAPLUS

DOCUMENT NUMBER: 119:15338

TITLE: New use of acidic polysaccharide esters as anti-ulcer

INVENTOR(S): agents  
 PATENT ASSIGNEE(S): Romeo, Aurelio; Toffano, Gino; Callegaro, Lanfranco  
 SOURCE: Fidia S.p.A., Italy  
 PCT Int. Appl., 41 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND   | DATE     | APPLICATION NO. | DATE     |
|---|--|----------|-----------------|----------|
| WO 9305792  | A1   | 19930401 | WO 1992-EP2133  | 19920914 |
| W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE |  |          |                 |          |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG    |  |          |                 |          |
| AU 9225481  | A1   | 19930427 | AU 1992-25481   | 19920914 |
| EP 605478   | A1   | 19940713 | EP 1992-919162  | 19920914 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE   |  |          |                 |          |
| US 5300493  | A  | 19940405 | US 1992-945495  | 19920916 |
| PRIORITY APPLN. INFO.:  |  |          | IT 1991-PD163   | 19910916 |
|   |  |          | WO 1992-EP2133  | 19920914 |
| AB  | Choline esters of acidic polysaccharides, such as hyaluronic acid, alginic acid, and CM cellulose, are effective as ulcer inhibitors and gastroprotective agents. Alginic acid choline ester (I) was orally administered to rats before reserpine injection; gastroprotective activity of I was dose-dependent and its efficacy was greater than that of sucralfate. A packet to mix with water before use comprised granules containing I 400, crosslinked Na CMC 450, colloidal silica 10, talc 30, aspartame 20, flavor q.s., and sucrose to 3500 mg. |          |                 |          |
| IC  | ICM A61K031-72   |          |                 |          |
| CC  | 63-6 (Pharmaceuticals)   |          |                 |          |
| IT  | <b>Pharmaceutical dosage forms</b><br>(granules, acidic polysaccharide choline esters in, for ulcer treatment)   |          |                 |          |
| IT  | <b>Pharmaceutical dosage forms</b><br>(tablets, acidic polysaccharide choline esters in, for ulcer treatment)  |          |                 |          |
| IT  | 9005-82-7, Amylose 9037-22-3, <b>Amylopectin</b><br>RL: BIOL (Biological study)<br>(starch containing, gastroprotective carboxyalkyl starch choline esters preparation from)   |          |                 |          |

L50 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1991:234939 HCAPLUS

DOCUMENT NUMBER: 114:234939

TITLE: Polysaccharide-coated oil droplets in oil-in-water emulsions as targetable carriers for lipophilic drugs  
 AUTHOR(S): Iwamoto, Kiyoshi; Kato, Takashi; Kawahara, Masahiro; Koyama, Noritoshi; Watanabe, Sumio; Miyake, Yasuo; Sunamoto, Junzo

CORPORATE SOURCE: Dep. Pharm. Res., Eisai Co., Ltd., Tsukuba, 300-26, Japan

SOURCE: Journal of Pharmaceutical Sciences (1991), 80(3), 219-24

CODEN: JPMSAE; ISSN: 0022-3549

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The surface of oil droplets in an oil-in-water (o/w) emulsion were coated

with naturally occurring polysaccharides (such as mannan, **amylopectin**, and pullulan) which were, in part, bearing a cholesterol moiety. The mean size of the colloidal droplets was not altered much, even by coating with the polysaccharide derivs., while the surface charge of the droplet decreased upon coating. Mannan and **amylopectin** derivative-coated droplets aggregated upon addition of Con A. These observations suggest that the terminal sugar moiety of the specific polysaccharides on the surface of colloidal droplets can be recognized by lectin. After i.v. **injection** of the emulsions into guinea pigs, kinetics of the blood clearance and the tissue distribution of the polysaccharide-coated oil droplets, which contain [<sup>14</sup>C]coenzyme Q10 as the marker, were investigated. In the initial rapid phase of blood clearance of the radioactivity, the polysaccharide-coated droplets were cleared from the blood stream slower than the uncoated ones. The lung uptake of the mannan derivative-coated droplet emulsion at 30 min after i.v. **injection** was .apprx.15 times higher than that of the conventional emulsion without the polysaccharide coat.

CC 63-5 (Pharmaceuticals)  
 Section cross-reference(s): 33  
 IT **Pharmaceutical** dosage forms  
 (emulsions, oil droplets coated with polysaccharide cholesterol derivs.  
 for, for targeting drugs)  
 IT 57-88-5D, Cholesterol, polysaccharide derivs. 9037-22-3D,  
**Amylopectin**, cholesteryl derivs. 9057-02-7D, Pullulan,  
 cholesteryl derivs.  
 RL: BIOL (Biological study)  
 (oil droplets coated with, for emulsions for targeting drugs)

L50 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 1984:73899 HCAPLUS  
 DOCUMENT NUMBER: 100:73899  
 TITLE: Improved drug delivery to target specific organs using  
 liposomes coated with polysaccharides  
 AUTHOR(S): Sunamoto, Junzo; Iwamoto, Kiyoshi; Takada, Masahiro;  
 Yuzuriha, Teruaki; Katayama, Kouichi  
 CORPORATE SOURCE: Fac. Eng., Nagasaki Univ., Nagasaki, 852, Japan  
 SOURCE: Polymer Science and Technology (Plenum) (1983),  
 23(Polym. Med.), 157-68  
 CODEN: POSTB5; ISSN: 0093-6286  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB An assembly of a cell wall-like structure on the outermost surface of liposomes was constructed, which makes liposomes tough against chemical and physicochem. lyses of liposomal membranes caused by external stimuli. Partly modified polysaccharides, O-palmitoylpullulan (OPP) [53572-58-0] and O-palmitoyl**amylopectin** (OPA) [86090-06-4] were used for coating the outermost surface of egg phosphatidylcholine liposomes. The efficiency of coating liposomes with the artificial cell wall was ascertained by 4 different methods: (1) isolation of polysaccharide-coated liposomes by gel-filtration, (2) reduced permeability for a water-soluble material, carboxyfluorescein, encapsulated in the interior of liposomes, (3) increased resistance against the enzymic lysis with phospholipase D for the coated liposomes, and (4) decreased probability in the enzymic digestion with pullulanase of the polysaccharide strongly bound to the surface of liposomes. This suggests a wide usage of the polysaccharide-coated liposomes as an improved drug carrier. When conventional liposomes are administered, they are highly distributed in liver and kidney in general because of their hydrophobic (lipophilic) character. However, <sup>14</sup>C-labeled CoQ10 [303-98-0] encapsulated in the

OPA-coated liposomes was more highly distributed in spleen and lung after i.v. **injection** through the femoral vein of male guinea pigs.

CC 63-6 (Pharmaceuticals)  
ST liposome coating pullulan **amylopectin**; delivery system drug liposome; polysaccharide liposome drug delivery  
IT **Pharmaceuticals**  
(delivery systems for, polysaccharide-coated liposomes as)

L50 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1980:191061 HCAPLUS

DOCUMENT NUMBER: 92:191061

TITLE: The catabolism of low molecular weight hydroxyethylated **amylopectin** in man. II. Changes in the urinary molecular profiles

AUTHOR(S): Mishler, John Milton; Ricketts, C. R.; Parkhouse, E. J.; Borberg, H.; Gross, R.

CORPORATE SOURCE: Med. Universitätsklin. Koeln, Cologne, 5000/41, Fed. Rep. Ger.

SOURCE: International Journal of Clinical Pharmacology, Therapy and Toxicology (1980), 18(1), 5-9  
CODEN: IJCPB5; ISSN: 0300-9718

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rates of urinary excretion concomitant with changes occurring in the mol. size distribution were determined in normal men dosed with 400 mL of a 14% solution of low-mol.-weight hydroxyethylated **amylopectin** [56448-79-4] (LMW-HES, mol. weight 264,000). Approx. 15% of the total infused LMW-HES was excreted in the urine during the 1st postinjection hour, and 50% by 24 h. Even though 15% of the total **injected** LMW-HES dose appeared in the urine 1 h postinfusion, the viscosity of the voided urine was only 30% above that of distilled H<sub>2</sub>O. The relation between urine viscosity and LMW-HES concentration was well described math. by the 1st-order equation:  $y = 0.774 + 0.0107x$ . Gel filtration using a column of CL-4B Sepharose showed that aliquots of urine collected postinjection contained mol.-weight fractions with lower values than the original **injected** LMW-HES, and with less polydispersity. Apparently, the catabolism of this material occurs in 2 distinct phases: a rapid initial hydrolysis, followed by a slow elimination influenced by the degree of hydroxyethylation.

CC 1-2 (Pharmacodynamics)

ST **amylopectin** hydroxyethyl catabolism urine;  
**hydroxyethylamylopectin** catabolism **pharmacokinetics**  
urine; starch hydroxyethyl catabolism urine

IT Urine  
(hydroxylated **amylopectin** excretion in, mol. weight in relation to)

IT Molecular weight  
(of hydroxylated **amylopectin**, catabolism and urinary excretion in relation to)

L50 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1977:444241 HCAPLUS

DOCUMENT NUMBER: 87:44241

TITLE: Use of 20,22-dihydrocardenolide glycosides in the treatment of blood circulation disorders

INVENTOR(S): Chaumann, Wolfgang; Dietmann, Karl; Bartsch, Wolfgang; Kaiser, Fritz; Voigtlaender, Wolfgang

PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Fed. Rep. Ger.

SOURCE: Ger. Offen., 14 pp.  
CODEN: GWXXBX

DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|------------|------|----------|-----------------|----------|
| DE 2546778 | A1   | 19770428 | DE 1975-2546778 | 19751018 |

PRIORITY APPLN. INFO.: DE 1975-2546778 19751018

AB **Pharmaceutical** compns. containing derivs. of 20,22-dihydrocardenolide glycosides are prepared for the treatment of blood circulatory disorders connected with cardiac failures. The compns. can be administered orally or **parenterally**. For example, tablets were formulated containing 20,22-dihydro- $\beta$ -methyldigoxin (I) [53152-57-1] 1.000, KH<sub>2</sub>PO<sub>4</sub> 2.694, Na<sub>2</sub>HPO<sub>4</sub> 1.306, lactose 73.100, polyvinylpyrrolidone 4.500, colloidal silicic acid 1.000, **amylopectin** glycolate Na 2.000, talc 4.000, and Mg stearate 0.400 g. The mixture was tableted, and each tablet contained 1 mg I.

IC A61K031-705

CC 63-6 (Pharmaceuticals)

L50 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1976:126762 HCAPLUS

DOCUMENT NUMBER: 84:126762

TITLE: **Pharmaceutical** preparation containing 5-(4-chloro-5-sulfamoyl-2-thenylaminophenyl)tetrazole and 3-(3-oxo-7 $\alpha$ -acetylthio-17 $\beta$ -hydroxy-4-androstene-17 $\alpha$ -yl)-propionic acid- $\gamma$ -lactone

INVENTOR(S): Kuhn, Rolf; Hardebeck, Klaus; Heinemann, Helmut

PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Fed. Rep. Ger.

SOURCE: Ger. Offen., 9 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|------------|------|----------|-----------------|----------|
| DE 2423606 | A1   | 19751127 | DE 1974-2423606 | 19740515 |
| US 4031213 | A    | 19770621 | US 1975-568640  | 19750416 |
| AU 7581023 | A1   | 19761111 | AU 1975-81023   | 19750509 |
| GB 1457481 | A    | 19761201 | GB 1975-19605   | 19750509 |
| NL 7505534 | A    | 19751118 | NL 1975-5534    | 19750512 |
| NL 156920  | B    | 19780615 |                 |          |
| BE 829023  | A1   | 19751113 | BE 1975-156310  | 19750513 |
| FR 2270869 | A1   | 19751212 | FR 1975-14988   | 19750514 |
| FR 2270869 | B1   | 19781006 |                 |          |

PRIORITY APPLN. INFO.: DE 1974-2423606 19740515

AB The preparation of oral or **parenteral pharmaceutical** formulations containing both 5-(4-chloro-5-sulfamoyl-2-thenylaminophenyl)tetrazole (I) [27589-33-9] and 3-(3-oxo-7 $\alpha$ -acetylthio-17 $\beta$ -hydroxy-4-androsten-17 $\alpha$ -yl)propionic acid  $\gamma$ -lactone (II) [52-01-7] or their salts for the treatment of hydropic conditions is described. I and II are both diuretics; given together, they enhance H<sub>2</sub>O and Na<sup>+</sup> excretion, but the presence of II inhibits the undesirable increase in K<sup>+</sup> excretion caused by I alone. I and II are present in the combined preparation in the ratios 1:5-10:5. Thus, a

micronized mixture of II 1000, lactose 2880, and Na lauryl sulfate 120 g was mixed with a preparation composed of I 300, lactose 1696, Na CM-**amylopectin** 200, and highly dispersed silicic acid 4 g. The total mixture was granulated, dried, and sieved, and the preparation was mixed with cornstarch 160 and Mg stearate 40 g. The final preparation was encapsulated or tabletted in 320-mg units, whereby each unit contained 15 mg I and 50 mg II.

IC A61K

CC 63-6 (Pharmaceuticals)

L50 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1943:882 HCAPLUS

DOCUMENT NUMBER: 37:882

ORIGINAL REFERENCE NO.: 37:182g-i,183a

TITLE: The **pharmacology** of sodium hydroxyacetate with observations on the toxicity of glycine

AUTHOR(S): Riker, Walter F.; Gold, Harry

SOURCE: Journal of the American Pharmaceutical Association (1912-1977) (1942), 31, 306-12  
CODEN: JPHAA3; ISSN: 0003-0465

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C. A. 36, 2026.7. Na hydroxyacetate is toxic for cats and dogs, and produces similar effects in both species. An oral dose of 0.1 g. per kg. rarely causes toxic effects; 0.25 g. per kg. is toxic, but not fatal; 0.5 g. per kg. (corresponding to about 35 g. for a man) may prove fatal. The absorption of Na hydroxyacetate from the gastrointestinal tract appears to be rather slow, but indications are that it is fairly complete. The onset of effects of Na hydroxyacetate is slow even after **intravenous injection**, the length of the latent period varying inversely with the dose. The course of action is protracted: in the typical case effects appear after about 30 min., progress in intensity during the next 24 hrs., and either subside gradually during the subsequent several days or increase in intensity and prove fatal in several days. The cat eliminates nontoxic doses within 24 hrs. or less; the recovery from toxic doses, however, is so slow as to suggest some impairment of elimination or an injury which progresses independently of the elimination of the drug. The symptoms of Na hydroxyacetate toxicity are anorexia, nausea and vomiting, neuromuscular disturbances, with weakness, ataxia, muscle twitching and convulsions. The drug exerts a nephrotoxic action resulting in tubular degeneration and marked elevation of the blood nonprotein N and creatinine. Limited comparisons with other organic acids showed that it is more toxic than fumaric, citric, acetic and aminoacetic acids. Glycine is toxic to cats and dogs, producing symptoms resembling in many respects those of Na hydroxyacetate, but not identical with the latter. The mechanism of action and metabolism of Na hydroxyacetate are discussed.

CC 11H (Biological Chemistry: Pharmacology)

IT Glycolic acid, sodium salt, compound with **amylopectin** (pharmacology of)